


1: AAW32305. Reports pol protein [Huma...[gi:57012029]

```
LOCUS       AAW32305                328 aa            linear   VRL 08-JAN-2005
DEFINITION  pol protein [Human immunodeficiency virus 1].
ACCESSION   AAW32305
VERSION     AAW32305.1  GI:57012029
DBSOURCE    accession AY845746.1
KEYWORDS    .
SOURCE      Human immunodeficiency virus 1 (HIV-1)
  ORGANISM  Human immunodeficiency virus 1
            Viruses; Retro-transcribing viruses; Retroviridae;
            Orthoretrovirinae; Lentivirus; Primate lentivirus group.
REFERENCE   1  (residues 1 to 328)
  AUTHORS   Carr,J.K., Nadai,Y., Saad,M.D., Khakimov,M.M., Yakubov,S.K.,
            Birx,D.L., Graham,R.R., Earhart,K. and Sanchez,J.L.
  TITLE     Outbreak of West African Recombinant of HIV-1 in Tashkent,
            Uzbekistan
  JOURNAL   Unpublished
REFERENCE   2  (residues 1 to 328)
  AUTHORS   Carr,J.K., Nadai,Y., Saad,M.D., Khakimov,M.M., Yakubov,S.K.,
            Birx,D.L., Graham,R.R., Earhart,K. and Sanchez,J.L.
  TITLE     Direct Submission
  JOURNAL   Submitted (03-DEC-2004) U.S. Military HIV Research Program, Henry
            M. Jackson Foundation, 1 Taft Court, Suite 250, Rockville, MD
            20850, USA
COMMENT     Method: conceptual translation.
FEATURES             Location/Qualifiers
     source          1..328
                     /organism="Human immunodeficiency virus 1"
                     /proviral
                     /isolate="03UZ010"
                     /isolation_source="26 year old male in 2003"
                     /db_xref="taxon:11676"
                     /country="Uzbekistan"
                     /note="subtype: A"
     Protein         <1..>328
                     /product="pol protein"
     mat_peptide     1..99
                     /product="protease"
     mat_peptide     100..>328
                     /product="reverse transcriptase"
     CDS             1..328
                     /gene="pol"
                     /coded_by="AY845746.1:<1..>985"
ORIGIN
        1 pqitlwqrpl vtvriggqlk ealldtgadd tvledinlpg kwkpkmiggi ggfikvrqyd
       61 qilieicgkk aigtvligpt pvniigrnml tqlgctlnfp ispietvpvt lkpgmdgprv
```

```
      121 kqwplteeki kalidickem ekegkisrig penpyntpif vikkkdstkw rklvdfreln
      181 krtqdfwevq lgiphpaglk kkksvtvldv gdayfsvpld esfrkytaft ipsinnetpg
      241 iryqynvlpq gwkgspsifq ssmtkilepf rlknpeiviy qymddlyvgs dleigqhrtk
      301 ieelrahlls wgfttpdkkh qkeppflw
//
```



Feb 9 2005 14:31:10




```
LOCUS       AAW37222                  104 aa            linear   BCT 27-APR-2005
DEFINITION  nitrite reductase [NAD(P)H], small subunit [Staphylococcus aureus
            subsp. aureus COL].
ACCESSION   AAW37222
VERSION     AAW37222.1  GI:57285128
DBSOURCE    accession CP000046.1
KEYWORDS    .
SOURCE      Staphylococcus aureus subsp. aureus COL
  ORGANISM  Staphylococcus aureus subsp. aureus COL
            Bacteria; Firmicutes; Bacillales; Staphylococcus.
REFERENCE   1  (residues 1 to 104)
  AUTHORS   Gill,S.R., Fouts,D.E., Archer,G.L., Mongodin,E.F., Deboy,R.T.,
            Ravel,J., Paulsen,I.T., Kolonay,J.F., Brinkac,L., Beanan,M.,
            Dodson,R.J., Daugherty,S.C., Madupu,R., Angiuoli,S.V., Durkin,A.S.,
            Haft,D.H., Vamathevan,J., Khouri,H., Utterback,T., Lee,C.,
            Dimitrov,G., Jiang,L., Qin,H., Weidman,J., Tran,K., Kang,K.,
            Hance,I.R., Nelson,K.E. and Fraser,C.M.
  TITLE     Insights on Evolution of Virulence and Resistance from the Complete
            Genome Analysis of an Early Methicillin-Resistant Staphylococcus
            aureus Strain and a Biofilm-Producing Methicillin-Resistant
            Staphylococcus epidermidis Strain
  JOURNAL   J. Bacteriol. 187 (7), 2426-2438 (2005)
   PUBMED   15774886
REFERENCE   2  (residues 1 to 104)
  AUTHORS   Gill,S., Fouts,D.E., Archer,G.L., Mongodin,E.F., DeBoy,R.T.,
            Ravel,J., Paulsen,I.T., Kolonay,J.F., Dodson,R.J., Durkin,A.S.,
            Brinkac,L., Beanan,M., Daugherty,S.C., Madupu,R., Angiuoli,S.V.,
            Haft,D.H., Vamathevan,J., Khouri,H.M., Utterback,T., Lee,C.,
            Dimitrov,G., Jiang,L., Qin,H., Weidman,J., Tran,K., Kang,K.,
            Hance,I., Nelson,K.E. and Fraser,C.M.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-NOV-2004) The Institute for Genomic Research, 9712
            Medical Center Dr, Rockville, MD 20850, USA
COMMENT     Method: conceptual translation.
FEATURES             Location/Qualifiers
     source          1..104
                     /organism="Staphylococcus aureus subsp. aureus COL"
                     /strain="COL"
                     /sub_species="aureus"
                     /db_xref="taxon:93062"
     Protein         1..104
                     /product="nitrite reductase [NAD(P)H], small subunit"
                     /EC_number="1.6.6.4"
     CDS             1..104
                     /gene="nirD"
```

```
                     /locus_tag="SACOL2397"
                     /old_locus_tag="SA2397"
                     /coded_by="complement(CP000046.1:2458192..2458506)"
                     /note="identified by similarity to EGAD:30823; match to
                     protein family HMM PF00355; match to protein family HMM
                     TIGR02378"
                     /transl_table=11
ORIGIN
        1 metkekikvt tideltplig kkvivkgkev glfltesgki haihnicphk qgplsegtvs
       61 geyvfcplhd qkidlntgiv qepdegcvdv yevevtdgnv yicl
//
```



Feb 9 2005 14:31:30

ile   5:Biosis Previews(R) 1969-2004/Oct W3
         (c) 2004 BIOSIS
File   6:NTIS 1964-2004/Oct W2
         (c) 2004 NTIS, Intl Cpyrght All Rights Res
File   8:Ei Compendex(R) 1970-2004/Oct W3
         (c) 2004 Elsevier Eng.  Info. Inc.
File  34:SciSearch(R) Cited Ref Sci 1990-2004/Oct W3
         (c) 2004 Inst for Sci Info
File  65:Inside Conferences 1993-2004/Oct W4
         (c) 2004 BLDSC all rts. reserv.
File  71:ELSEVIER BIOBASE 1994-2004/Oct W3
         (c) 2004  Elsevier Science B.V.
File  73:EMBASE 1974-2004/Oct W3
         (c) 2004 Elsevier Science B.V.
File  94:JICST-EPlus 1985-2004/Sep W4
         (c)2004 Japan Science and Tech Corp(JST)
File  98:General Sci Abs/Full-Text 1984-2004/Sep
         (c) 2004 The HW Wilson Co.
File  99:Wilson Appl. Sci & Tech Abs 1983-2004/Sep
         (c) 2004 The HW Wilson Co.
File 135:NewsRx Weekly Reports 1995-2004/Oct W3
         (c) 2004 NewsRx
File 143:Biol. & Agric. Index 1983-2004/Aug
         (c) 2004 The HW Wilson Co
File 144:Pascal 1973-2004/Oct W3
         (c) 2004 INIST/CNRS
File 155:MEDLINE(R) 1951-2004/Oct W4
         (c) format only 2004 The Dialog Corp.
File 172:EMBASE Alert 2004/Oct W3
         (c) 2004 Elsevier Science B.V.
File 266:FEDRIP 2004/Aug
         Comp & dist by NTIS, Intl Copyright All Rights Res
File 315:ChemEng & Biotec Abs 1970-2004/Sep
         (c) 2004 DECHEMA
File 357:Derwent Biotech Res. _1982-2004/Oct W5
         (c) 2004 Thomson Derwent & ISI
File 358:Current BioTech Abs 1983-2004/Sep
          (c) 2004 DECHEMA
File 369:New Scientist 1994-2004/Oct W3
         (c) 2004 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
         (c) 1999 AAAS
File 399:CA SEARCH(R) 1967-2004/UD=14118
         (c) 2004 American Chemical Society
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File  40:Enviroline(R) 1975-2004/Aug
File  50:CAB Abstracts 1972-2004/Sep
         (c) 2004 CAB International
File 103:Energy SciTec 1974-2004/Oct B1
         (c) 2004 Contains copyrighted material
File 156:ToxFile 1965-2004/Oct W4
         (c) format only 2004 The Dialog Corporation
File 162:Global Health 1983-2004/Sep
         (c) 2004 CAB International
File 305:Analytical Abstracts 1980-2004/Oct W3
         (c) 2004 Royal Soc Chemistry
File 393:Beilstein Abstracts  July 2004
         (c) 2004 Beilstein GmbH
File  35:Dissertation Abs Online 1861-2004/Sep
         (c) 2004 ProQuest Info&Learning
File  48:SPORTDiscus 1962-2004/Nov
         (c) 2004 Sport Information Resource Centre
File  91:MANTIS(TM) 1880-2004/Oct
         2001 (c) Action Potential
File 149:TGG Health&Wellness DB(SM) 1976-2004/Oct W2
         (c) 2004 The Gale Group

File 159:Cancerlit 1975-2002/Oct
(c) format only 2002 Dialog Corporation
File 164:Allied & Complementary Medicine 1984-2004/Oct
(c) 2004 BLHCIS
File 444:New England Journal of Med. 1985-2004/Oct W3
(c) 2004 Mass. Med. Soc.
File 467:ExtraMED(tm) 2000/Dec
(c) 2001 Informania Ltd.

| Set | Items | Description |
|---|---|---|
| S1 | 186 | (CYCLIC (3N) PEPTIDE?) (S) ADVANTAGE? |
| S2 | 101 | RD (unique items) |
| S3 | 4 | S2 AND LACTAM? |

>>>KWIC option is not available in file(s): 399

**3/3,K/1 (Item 1 from file: 34)**
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


05120441 Genuine Article#: VB464 No. References: 55
**Title: ENHANCEMENT OF THE INTESTINAL-ABSORPTION OF PEPTIDES AND NONPEPTIDES**
Author(s): AUNGST BJ; SAITOH H; BURCHAM DL; HUANG SM; MOUSA SA; HUSSAIN MA
Corporate Source: DUPONT MERCK PHARMACEUT CO,POB 80400/WILMINGTON//DE/19880
Journal: JOURNAL OF CONTROLLED RELEASE, 1996, V41, N1-2 (AUG), P19-31
ISSN: 0168-3659
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

...Abstract: The literature on permeation enhancement with these agents is briefly reviewed. We evaluated permeation enhancement approaches to increase the oral bioavailability of a non-metabolized, *cyclic* *peptide* fibrinogen antagonist, DMP 728. Sodium caprate (15 mM) increased the in vitro intestinal permeation rate 3-fold. Oral absorption in dogs was also increased approximately...
...bioavailability in rats. However, oral bioavailability of DuP 532 in rats and dogs was increased approximately 3-fold using glyceride vehicles. These excipients have the *advantage* of already being used in marketed products. As with DMP 728, there was substantial inter-animal variability of DuP 532 oral bioavailability, and optimization of...
...Identifiers--POORLY ABSORBED DRUGS; EPITHELIAL CACO-2 CELLS; MEDIUM-CHAIN GLYCERIDES; BETA-*LACTAM* ANTIBIOTICS; SODIUM CAPRATE; RECTAL ABSORPTION; BILE-SALTS; RAT COLON; PERMEABILITY ENHANCEMENT; MEMBRANE PERMEATION

**3/3,K/2 (Item 1 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0341720 DBR Accession No.: 2004-14012 PATENT
**Novel tumor targeting unit, useful for treating cancer or cancer related disease e.g., solid tumor such as carcinoma, sarcoma, melanoma or metastasis - a resin bound protein preparation comprising a detectable and therapeutic agent useful in cancer therapy**
AUTHOR: BERGMAN M; AUVINEN M; ELO H
PATENT ASSIGNEE: KARYON OY 2004
PATENT NUMBER: WO 200431218 PATENT DATE: 20040415 WPI ACCESSION NO.: 2004-347955 (200432)
PRIORITY APPLIC. NO.: FI 20021763 APPLIC. DATE: 20021003
NATIONAL APPLIC. NO.: WO 2003FI723 APPLIC. DATE: 20031003
LANGUAGE: English

...ABSTRACT: I) coupled to an effector unit; and (2) a diagnostic (III) or pharmaceutical composition (IV), comprising (I) or (II). BIOTECHNOLOGY - Preferred Unit: In (I), the *peptide* is *cyclic* or forms part of a cyclic structure. The cyclic structure is formed by a *lactam* or

lactone bond. (I) is derivatized, activated, protected, resin bound or other support bound. Preferred Agent: In (II), the effector unit is a directly or...
... claimed). (III) is useful for diagnosing tumor. ADMINISTRATION - Administration of (IV) is 0.000001 microg/kg-40 mg/kg, systemically, non-systemically, locally or topically. *ADVANTAGE* - (I) and (II) are highly selective and have potent targeting ability. EXAMPLE - No example given.(106 pages)

**3/3,K/3 (Item 1 from file: 393)**
DIALOG(R)File 393:Beilstein Abstracts


**Beilstein Abstract Id: 6399826**
Title: Utilization of a beta -Aminophosphotyrosyl Mimetic in the Design and Synthesis of Macrocyclic Grb2 SH2 Domain-Binding Peptides
Document Type: Journal Record Type: Abstract
Author: Lee, Kyeong; Zhang, Manchao; Liu, Hongpeng; Yang, Dajun; Burke, Terrence R.
Citation: J.Med.Chem. (2003) Series: 46-13, 2621 - 2630 CODEN: JMCMAR
Language: English
Abstract Language: English

...Abstract: by several groups as potential new therapies for a variety of diseases, including certain cancers. In these efforts, macrocyclization has been successfully utilized to take *advantage* of preferential recognition by Grb2 SH2 domains of ligands in beta -bend conformations. Recent examples of this approach include olefin-metathesis-derived macrocycles that employ...

... stable beta -amino-pTyr mimetic designated "Pmp beta " was utilized to prepare variants of previously reported olefin-metathesis-deriv ed macrocycles. An initial set of simplified *cyclic* *peptides* lacking key naphthyl side chain functionality was first synthesized to determine optimum ring size, with results indicating that a four-unit ring-closing segment was appropriate. On the basis of these findings, *macrolactamization* was undertaken with a more highly functionalized, naphthyl-containing gamma -amino acid analogue. The resulting *cyclic* beta -amino *peptide* is the first of a new class of pTyr-mimetic-containing ligands that may have utility in the development of antagonists of both Grb2 SH2...

**3/3,K/4 (Item 2 from file: 393)**
DIALOG(R)File 393:Beilstein Abstracts


**Beilstein Abstract Id: 6168931**
Title: Total Synthesis and Conformational Studies of Hapalosin, N-Desmethylhapalosin and 8-Deoxyhapalosin
Document Type: Journal Record Type: Abstract
Author: Wagner, Bjoern; Gonzalez, Gabriel Islas; Dau, Marie Elise Tran Hun; Zhu, Jieping
Citation: Bioorg.Med.Chem. (1999) Series: 7-5, 737 - 748 CODEN: BMECEP
Language: English
Abstract Language: English

Abstract: Hapalosin (2), a 12-membered *cyclic* *depsipeptide* possessing MDR-reversing activity, and analogues (3) and (4) have been synthesized using *macrolactamization* as an important ring-forming step. Three building blocks: (2S,3R)-3-(tert-butyl dimethylsilyloxy)-2-methyl-decanoic acid (13), benzyl (S)-2-hydroxy-3-methylbutanate...

... and were assembled together by applying twice Yamaguchi's coupling methodology.A new and efficient selective N-methylation of gamma -hydroxy- beta -amino ester taking *advantage* of the vicinal amino alcohol funct ion was uncovered in the course of this study. Thus, treatment of compound 19 with HCHO in the presence...

?

S7 29 RD (unique items)

```
?show files;ds;t/3,k/all
File   5:Biosis Previews(R) 1969-2004/Oct W3
         (c) 2004 BIOSIS
File   6:NTIS 1964-2004/Oct W2
         (c) 2004 NTIS, Intl Cpyrght All Rights Res
File   8:Ei Compendex(R) 1970-2004/Oct W3
         (c) 2004 Elsevier Eng.  Info. Inc.
File  34:SciSearch(R) Cited Ref Sci 1990-2004/Oct W3
         (c) 2004 Inst for Sci Info
File  65:Inside Conferences 1993-2004/Oct W4
         (c) 2004 BLDSC all rts. reserv.
File  71:ELSEVIER BIOBASE 1994-2004/Oct W3
         (c) 2004  Elsevier Science B.V.
File  73:EMBASE 1974-2004/Oct W3
         (c) 2004 Elsevier Science B.V.
File  94:JICST-EPlus 1985-2004/Sep W4
         (c)2004 Japan Science and Tech Corp(JST)
File  98:General Sci Abs/Full-Text 1984-2004/Sep
         (c) 2004 The HW Wilson Co.
File  99:Wilson Appl. Sci & Tech Abs 1983-2004/Sep
         (c) 2004 The HW Wilson Co.
File 135:NewsRx Weekly Reports 1995-2004/Oct W3
         (c) 2004 NewsRx
File 143:Biol. & Agric. Index 1983-2004/Aug
         (c) 2004 The HW Wilson Co
File 144:Pascal 1973-2004/Oct W3
         (c) 2004 INIST/CNRS
File 155:MEDLINE(R) 1951-2004/Oct W4
         (c) format only 2004 The Dialog Corp.
File 172:EMBASE Alert 2004/Oct W3
         (c) 2004 Elsevier Science B.V.
File 266:FEDRIP 2004/Aug
         Comp & dist by NTIS, Intl Copyright All Rights Res
File 315:ChemEng & Biotec Abs 1970-2004/Sep
         (c) 2004 DECHEMA
File 357:Derwent Biotech Res. _1982-2004/Oct W5
         (c) 2004 Thomson Derwent & ISI
File 358:Current BioTech Abs 1983-2004/Sep
          (c) 2004 DECHEMA
File 369:New Scientist 1994-2004/Oct W3
         (c) 2004 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
         (c) 1999 AAAS
File 399:CA SEARCH(R) 1967-2004/UD=14118
         (c) 2004 American Chemical Society
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File  40:Enviroline(R) 1975-2004/Aug
File  50:CAB Abstracts 1972-2004/Sep
         (c) 2004 CAB International
File 103:Energy SciTec 1974-2004/Oct B1
         (c) 2004 Contains copyrighted material
File 156:ToxFile 1965-2004/Oct W4
         (c) format only 2004 The Dialog Corporation
File 162:Global Health 1983-2004/Sep
         (c) 2004 CAB International
File 305:Analytical Abstracts 1980-2004/Oct W3
         (c) 2004 Royal Soc Chemistry
File 393:Beilstein Abstracts  July 2004
         (c) 2004 Beilstein GmbH
File  35:Dissertation Abs Online 1861-2004/Sep
         (c) 2004 ProQuest Info&Learning
File  48:SPORTDiscus 1962-2004/Nov
         (c) 2004 Sport Information Resource Centre
File  91:MANTIS(TM) 1880-2004/Oct
         2001 (c) Action Potential
```

File 149:TGG Health&Wellness DB(SM) 1976-2004/Oct W2
(c) 2004 The Gale Group
File 159:Cancerlit 1975-2002/Oct
(c) format only 2002 Dialog Corporation
File 164:Allied & Complementary Medicine 1984-2004/Oct
(c) 2004 BLHCIS
File 444:New England Journal of Med. 1985-2004/Oct W3
(c) 2004 Mass. Med. Soc.
File 467:ExtraMED(tm) 2000/Dec
(c) 2001 Informania Ltd.

| Set | Items | Description |
|---|---|---|
| S1 | 186 | (CYCLIC (3N) PEPTIDE?) (S) ADVANTAGE? |
| S2 | 101 | RD (unique items) |
| S3 | 4 | S2 AND LACTAM? |
| S4 | 0 | S2 AND (REVIEW ARTICLE) |
| S5 | 0 | S2 AND (SIGNIFICAN? (S) (CYCLIC PEPTIDE?)) |
| S6 | 29 | S2 AND INHIBIT? |
| S7 | 29 | RD (unique items) |

>>>KWIC option is not available in file(s): 399

**7/3,K/1 (Item 1 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0014930707 BIOSIS NO.: 200400301464
**Synthetic peptide derived from alpha-fetoprotein *inhibits* growth of human breast cancer: investigation of the pharmacophore and synthesis optimization**
AUTHOR: DeFreest L A; Mesfin F B; Joseph L; McLeod D J; Stallmer A; Reddy S ; Balulad S S; Jacobson H I; Andersen T T; Bennett J A (Reprint)
AUTHOR ADDRESS: Ctr Immunol and Microbial Dis, Albany Med Coll, 47 New Scotland Ave MC 62,ME515, Albany, NY, 12208, USA**USA
AUTHOR E-MAIL ADDRESS: bennetj@mail.amc.edu
JOURNAL: Journal of Peptide Research 63 (5): p409-419 May 2004 2004
MEDIUM: print
ISSN: 1397-002X _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

**Synthetic peptide derived from alpha-fetoprotein *inhibits* growth of human breast cancer: investigation of the pharmacophore and synthesis optimization**

ABSTRACT: A synthetic peptide that *inhibits* the growth of estrogen receptor positive (ER+) human breast cancers, growing as xenografts in mice, has been reported. The cyclic 9-mer peptide, cyclo(EMTOVNOGQ...

...peptide, a series of analogs was prepared using solid-phase peptide synthesis. Analogs were screened in a 1-day bioassay, which assessed their ability to *inhibit* the estrogen-stimulated growth of uterus in immature mice. Deletion of glutamic acid, Glu1, abolished activity of the peptide, but glutamine (Gln) or asparagine (Asn...

...cancer activity equivalent to that of the original Met-containing peptide. Therefore, Met2 is not essential for biologic activity and substitution of Lys is synthetically *advantageous*. Threonine (Thr3) is a nonessential site, and can be substituted with serine (Ser), valine (Val), or alanine (Ala) without significant loss of activity. Hydroxyproline (Hyp...

...The results of this study provide information that will be helpful in the rational modification of cyclo(EMTOVNOGQ) to yield peptide analogs and peptidomimetics with *advantages* in synthesis, pharmacologic properties, and biologic activity.

7/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


0013741210 BIOSIS NO.: 200200334721
**Antiproliferative activity of microsclerodermins**
AUTHOR: Wright Amy E (Reprint); Pomponi Shirley A; Longley Ross E; Isbrucker Richard A
AUTHOR ADDRESS: Ft. Pierce, FL, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1258 (1): May 7, 2002 2002
MEDIUM: e-file
PATENT NUMBER: US 6384187 PATENT DATE GRANTED: May 07, 2002 20020507
PATENT CLASSIFICATION: 530-317 PATENT ASSIGNEE: Harbor Branch Oceanographic Institution, Inc. PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The subject invention pertains to a series of cyclic peptides known as the microsclerodermins, which possess unusual amino acids, and which have been observed to *inhibit* the proliferation of tumor cell lines. The subject invention also pertains to methods useful in *inhibiting* pathological cellular proliferation in animals, including humans and other mammals. In accordance with the teachings of the subject invention, microsclerodermin compounds can be used to *inhibit* cellular proliferation including that which is responsible for tumors and other cancers. In a specific embodiment, the novel compositions and methods of use of the subject invention can *advantageously* be useful in the treatment of a patient hosting cancer cells, for example, *inhibiting* the growth of tumor cells in a mammalian host.

7/3,K/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


0013587039 BIOSIS NO.: 200200180550
**Targeting adenoviral vectors by using the extracellular domain of the coxsackie-adenovirus receptor: Improved potency via trimerization**
AUTHOR: Kim Jin; Smith Theodore (Reprint); Idamakanti Neeraja; Mulgrew Kathy; Kaloss Michele; Kylefjord Helen; Ryan Patricia C; Kaleko Michael; Stevenson Susan C (Reprint)
AUTHOR ADDRESS: Genetic Therapy, Inc., A Novartis Company, 9 W. Watkins Mill Rd., Gaithersburg, MD, 20878, USA**USA
JOURNAL: Journal of Virology 76 (4): p1892-1903 February, 2002 2002
MEDIUM: print
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: molecules with soluble CAR (sCAR), which is the extracellular domain of CAR fused to peptide-targeting ligands. Two peptide-targeting ligands have been evaluated: a *cyclic* RGD *peptide* (cRGD) and the receptor-binding domain of apolipoprotein E (ApoE). Human diploid fibroblasts (HDF) are poorly transduced by adenovirus due to a lack of CAR...
...isoleucine GCN4 trimerization domain was introduced, and trimerization was verified by cross-linking analysis. Trimerized sCAR proteins were significantly better at interacting with fiber and *inhibiting* binding to HeLa cells. Trimeric sCAR proteins containing cRGD and ApoE were more efficient at transducing HDF in vitro than the monomeric proteins. In addition...

**7/3,K/4 (Item 4 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0012010777 BIOSIS NO.: 199900270437
**A mimic of HIV-1 nucleocapsid protein impairs reverse transcription and displays antiviral activity**
AUTHOR: Druillennec S; Dong C Z; Escaich S; Gresh N; Bousseau A; Roques B P (Reprint); Fournie-Zaluski M C
AUTHOR ADDRESS: Departement de Pharmacochimie Moleculaire et Structurale, U 266 Institut National de la Sante et de la Recherche Medicale, 4 Avenue de l'Observatoire, 75270, Paris Cedex 06, France**France
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 96 (9): p4886-4891 April 27, 1999 1999
MEDIUM: print
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Combined *inhibition* of HIV-1 reverse transcriptase and protease has significantly improved the treatment of AIDS. Nevertheless, resistance to these drugs occurs rapidly because of viral mutations...

...on these structural data, we report that RB 2121, a cyclic peptide designed to mimic several essential biological determinants of NCp7, displays antiviral activity by *inhibiting* HIV-1 replication in CEM-4 cells infected by HIV-1. In vitro, RB 2121 does not interfere with HIV-1 cell entry and viral enzymes but is able to *inhibit* the annealing activities of NCp7 by recognizing nucleic acids. Analysis of proviral DNA synthesis by means of PCR has shown that RB 2121 acts at an early step of the retrovirus life cycle by inducing a dose-dependent reduction in transcribed DNA levels through *inhibition* of NCp7-reverse transcriptase interaction. Because of its original mechanism of action, RB 2121 provides an interesting lead for the rational development of new anti-HIV-1 agents that could be associated *advantageously* with enzyme *inhibitors* to counteract rapid virus mutations and resistance problems observed in tritherapies.

**7/3,K/5 (Item 5 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0011913316 BIOSIS NO.: 199900172976
**Development of non-phosphorylated cyclic thioether peptide binding to the Grb2-SH2 domain**
AUTHOR: Lung Feng-Di T; King C Richter; Roller Peter P (Reprint)
AUTHOR ADDRESS: Laboratory of Medicinal Chemistry, National Cancer Institute, NIH, Building 37, Room 5C-02, Bethesda, MD, 20892-4255, USA** USA
JOURNAL: Letters in Peptide Science 6 (1): p45-49 Jan., 1999 1999
MEDIUM: print
ISSN: 0929-5666
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: in receptors and other cognate proteins. Following the lead of our recent findings that a phage library based non-phosphorylated disulfide linked 11-mer peptide *inhibited* such interactions, we report here the synthesis of novel redox-stable cyclic peptide analogs. These include thioether cyclized and backbone cyclized structures. The thioether analog...
...the Grb2-SH2 domain (IC50 = 10-15 muM) when compared to the disulfide cyclized lead-peptide. The bioactive thioether linked peptide was

demonstrated to offer *advantages* to the disulfide cyclized peptides under physiological conditions.

**7/3,K/6 (Item 6 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0009529124 BIOSIS NO.: 199497550409
**Ro 25-1553: A novel, long-acting vasoactive intestinal peptide agonist: Part II: Effect on in vitro and in vivo models of pulmonary anaphylaxis**
AUTHOR: O'Donnell M; Garippa R J; Rinaldi N; Selig W M; Tocker J E; Tannu S A; Wasserman M A (Reprint); Welton A; Bolin D R
AUTHOR ADDRESS: Hoffmann-La Roche Inc., 340 Kingsland St., Build. 76, Room 926A, Nutley, NJ 07119, USA**USA
JOURNAL: Journal of Pharmacology and Experimental Therapeutics 270 (3): p 1289-1294 1994 1994
ISSN: 0022-3565
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: 0.1-100 mu-g), instilled intratracheally 2 min before the antigen challenge of buffer-perfused lungs from sensitized guinea pigs, produced a dose-dependent *inhibition* of bronchoconstrictor, vasoconstrictor and edemagenic responses, whereas intratracheal VIP (100 mu-g) had no effect. Intratracheal salbutamol (0.1-100 mu-g) *inhibited* antigen-induced responses in a manner comparable to Ro 25-1553. Lung inflammation was assessed as leukocyte accumulation in bronchoalveolar lavage fluid after the antigen...

...Ro 25-1553 suppresses various pathophysiological features associated with pulmonary anaphylaxis and asthma, including airway reactivity, edema formation and granulocyte accumulation. By combining the clinical *advantages* of bronchodilation and anti-inflammatory activity, Ro 25-1553 could provide novel and more effective pharmacotherapy for the treatment of bronchial asthma.

**7/3,K/7 (Item 7 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0009529123 BIOSIS NO.: 199497550408
**Ro 25-1553: A novel, long-acting vasoactive intestinal peptide agonist: Part I: In vitro and in vivo bronchodilator studies**
AUTHOR: O'Donnell M; Garippa R J; Rinaldi N; Selig W M; Simko B; Renzetti L ; Tannu S A; Wasserman M A (Reprint); Welton A; Bolin D R
AUTHOR ADDRESS: Hoffmann-La Roche Inc., 340 Kingsland St., Build. 76, Room 926A, Nutley, NJ 07110, USA**USA
JOURNAL: Journal of Pharmacology and Experimental Therapeutics 270 (3): p 1282-1288 1994 1994
ISSN: 0022-3565
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: evident after in vivo intratracheal administration or aerosolization of the compound. Pulmonary responses evoked by histamine, leukotriene D-4, platelet-activating factor and acetylcholine are *inhibited* dose-dependently by intratracheally instilled Ro 25-1553 with nearly identical potency (ED-50 values ranging from 0.07 mu-g to 0.26 mu-g). Likewise, histamine-induced increases in lung resistance were concentration-dependently *inhibited* by aerosolized Ro 25-1553 (EC-50 = 0.001%). Time-course studies show a rapid onset of bronchodilator activity and a duration of approximately 180...

...concentration of 0.1% is administered. The combined properties of high biopotency and long-lasting bronchodilator activity may afford Ro 251553 distinct pharmacokinetic and therapeutic *advantages* over VIP and make it a promising candidate for clinical evaluation.

**7/3,K/8 (Item 8 from file: 5)**
DIALOG(R)File 5:Biosis Previews(R)


0005663997 BIOSIS NO.: 198784018146
**STRUCTURE REFINEMENT OF A CYCLIC PEPTIDE FROM TWO-DIMENSIONAL NMR DATA AND MOLECULAR MODELING**
AUTHOR: FESIK S W (Reprint); BOLIS G; SHAM H L; OLEJNICZAK E T
AUTHOR ADDRESS: PHARM DISCOVERY DIV, ABBOTT LAB, ABBOTT PARK, IL 60064, USA **USA
JOURNAL: Biochemistry 26 (7): p1851-1859 1987
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

Tear off

...ABSTRACT: methods included interactive manual manipulation of the structure to fit the NMR-determined distance constraints, distance geometry, constrained energy minimizations, and contrained molecular dynamics. The *advantages* and disadvantages of the methods are discussed. In addition, to gain insight into the conformations accessible to the *cyclic* *peptide* and the relative flexibility of the different parts of the molecule, molecular dynamics calculations were performed at three different temperatures. Average interproton distances and dihedral
...
...generated in the dynamics trajectories and compared to those obtained from the NMR experiments. Despite the four methylene groups and ether linkage contained in the *cyclic* portion of the *peptide*, our NMR results indicated a preferred conformation for the macrocyclic ring of the peptide and supported the presence of a cis Phe-Ala peptide bond...

...data indicated a considerable amount of flexibility for the remaining noncyclic portion of the molecule. These results are used to propose an explanation for the *cyclic* *peptide*'s inability to *inhibit* human renin.
DESCRIPTORS: HUMAN RENIN *INHIBITION* INABILITY ANTIHYPERTENSIVE AGENT DESIGN

**7/3,K/9 (Item 1 from file: 6)**
DIALOG(R)File 6:NTIS


1712540 NTIS Accession Number: AD-P008 547/2
**Design and Synthesis of Conformationally Restricted Renin *Inhibitors***
Brotherton-Pleiss, C. E. ; Newman, S. R. ; Waterbury, L. D. ; Schwartzberg, M. S.
Syntex (USA), Inc., Palo Alto, CA. Research Div.
Corp. Source Codes: 086094001; 424606
1992 2p
Languages: English
Journal Announcement: GRAI9310
This Article is from 'Peptides, Chemistry and Biology: Proceedings of the American Peptide Symposium (12th) Held in Cambridge, Massachusetts on 16-21 June 1991', AD-A256 113, p816-817.
Order this product from NTIS by: phone at 1-800-553-NTIS (U.S. customers); (703)605-6000 (other countries); fax at (703)321-8547; and email at orders@ntis.fedworld.gov. NTIS is located at 5285 Port Royal Road, Springfield, VA, 22161, USA.
NTIS Prices: PC A01/MF A01

**Design and Synthesis of Conformationally Restricted Renin *Inhibitors***

Constrained *cyclic* *peptides* have shown to be useful probes in the exploration of the conformational features of the peptide necessary for binding. In designing conformationally restricted analogs of...

...conformation and contain two hydrophobic side chains on the same side, a constraint that covalently links these side chains with a hydrophobic spacer offers the *advantage* of maintaining hydrogen bonds between the backbone of the *inhibitor* and the enzyme while maximizing the hydrophobic interactions of the side chains and the binding properties of the individual side chains.

Descriptors: Renin; *Enzyme *inhibitors*; Peptide hydrolases; Amino acids ; Angiotensin; Hydrophobic properties; Cyclic compounds

Identifiers: Cyclic renin *inhibitors*; Component Reports; Synthesis(Chemistry); NTISDODXA

ICC

**7/3,K/10 (Item 1 from file: 34)**



10613595 Genuine Article#: 547PK No. References: 126

**Title: Development of short antimicrobial peptides derived from host defense peptides or by combinatorial libraries**

Author(s): Lee KH (REPRINT)
Corporate Source: Inha Univ,Dept Chem,253 Younghyong Dong/Inchon 402751//South Korea/ (REPRINT); Inha Univ,Dept Chem,Inchon 402751//South Korea/

Journal: CURRENT PHARMACEUTICAL DESIGN, 2002, V8, N9, P795-813
ISSN: 1381-6128 Publication date: 20020000
Publisher: BENTHAM SCIENCE PUBL LTD, PO BOX 1673, 1200 BR HILVERSUM, NETHERLANDS
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

...Abstract: molecules with unexploited mechanisms. Several hundred host defense peptides have been isolated from natural sources and their functions characterized. As host defense peptides have several *advantages* over classic antibiotics for resistant pathogens, there are many efforts to develop host defense peptides as therapeutic agents. In this review, focusing on the development of short antimicrobial peptides (less than or equal to18-mer), several examples are introduced that identify the active fragment from *cyclic* host *peptides*, or novel antimicrobial peptides derived from combinatorial libraries. Moreover, structure-activity relationships of short antimicrobial peptides are discussed, and several methods for improving bioavailability as...

...Identifiers--MEMBRANE-ACTIVE PEPTIDE; PERMEABILITY-INCREASING PROTEIN; HELICOBACTER-PYLORI INFECTION; NUCLEAR-MAGNETIC-RESONANCE; CELL FUSION *INHIBITOR*; PEREGRINA FLESH FLY; ANTIBACTERIAL PROTEIN; SECONDARY STRUCTURE; INSECT DEFENSIN; SARCOPHAGA-PEREGRINA

**7/3,K/11 (Item 2 from file: 34)**



09927411 Genuine Article#: 465RK No. References: 12

**Title: Phage derived peptides for targeting of doxorubicin conjugates to solid tumours**

Author(s): Schatzlein AG (REPRINT) ; Rutherford C; Corrihons F; Moore BD
Corporate Source: Univ Glasgow,CRC, Dept Med Oncol,Glasgow G61 1BD/Lanark/Scotland/ (REPRINT); Univ Glasgow,CRC, Dept Med Oncol,Glasgow G61 1BD/Lanark/Scotland/; Univ Strathclyde,Dept Pure & Appl Chem,Glasgow/Lanark/Scotland/

Journal: JOURNAL OF CONTROLLED RELEASE, 2001, V74, N1-3 (JUL 6), P357-362
ISSN: 0168-3659 Publication date: 20010706
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS

Language: English  Document Type: ARTICLE  (ABSTRACT AVAILABLE)

...Abstract: conjugates are low molecular weight conjugates of a small drug or toxin and a targeting ligand coupled through a cleavable linker group. They offer potential *advantages* for tumour specific delivery in diffusion-limited situations. We have exploited fd phage-derived peptides for the targeting of low molecular weight drug conjugates to solid tumours. As a model we have chosen doxorubicin conjugates targeted to the transferrin receptor (TfR). A library of phage expressing a *cyclic* nona-*peptide* was panned against TfR. The apparent affinity of phages determined by surface plasmon resonance (SPR) increased with each cycle of the panning procedure. After five...

...using solid phase peptide chemistry on a sulfonamide based safety catch resin. Crude mixtures of the peptide, as well as transferrin itself. were able to *inhibit* the phage uptake significantly. The doxorubicin conjugate of the peptide containing a cleavable linker was prepared and endosomal uptake confirmed by fluorescence microscopy. (C) 2001...

**7/3,K/12  (Item 1 from file: 266)**
DIALOG(R)File 266:FEDRIP


00320709
IDENTIFYING NO.: 1R01AI053800-01  AGENCY CODE: CRISP
**INTRACELLULAR CYCLIC PEPTIDE LIBRARIES**
PRINCIPAL INVESTIGATOR: SCOTT, CHARLES P
ADDRESS: CHARLES.SCOTT@MAIL.TJU.EDU SCOTT, CHARLES 233 SOUTH 10TH ST, RM 833 PHILADELPHIA, PA 19107
PERFORMING ORG.: THOMAS JEFFERSON UNIVERSITY, PHILADELPHIA, PENNSYLVANIA
SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
DATES: 2012/01/02 TO 2011/30/07  FY : 2003

SUMMARY: DESCRIPTION (provided by applicant): The research program described in this application is focused on development of intracellular libraries of *cyclic* *peptides* as sources of molecular diversity for drug discovery and chemical genetics. Intracellular peptide and protein cyclization is made possible through circular permutation of inteins (internal proteins). Thus far we have used the technology to elaborate vast, chemically diverse libraries of low molecular weight *cyclic* *peptide* in bacterial host cells. To transform these libraries into a comprehensive, cross-cutting technology that can be translated into a variety of biomedical applications, we will: 1) demonstrate that intracellular *cyclic* *peptide* libraries can be used to generate high affinity ligands to a selected target receptor; 2) validate peptide cyclization technology in eukaryotic and mammalian cell hosts, which are most relevant for biomedical research; and 3) develop general strategies that enable facile identification of physiological targets that interact with *cyclic* *peptides* effectors in cells. My laboratory will pursue a protein engineering approach to these objectives, and implement the improvements as part of a program to discover small molecules that *inhibit* replication of hepatitis C virus (HCV). We will take *advantage* of existing libraries in bacterial hosts by creating a high throughput screen to identify potent *inhibitors* of a heterologously expressed HCV gene product (aim 1). We will optimize intein-mediated cyclization in mammalian host cells and evaluate compatibility of cyclization with...

... localization (aim 2). We will modify the selection marker of the HCV replicon for greater versatility in chemical genetics studies of viral pathogenesis and transfer *cyclic* *peptide* *inhibitors* identified by screening bacterial libraries into the modified HCV replicon to evaluate their effects on viral replication in hepatocytes (aim 3). Finally, We will engineer...

...two hybrid systems, explore two hybrid systems, expression libraries and affinity based methods for peptide target identification and initiate

studies to identify new viral replication *inhibitors* and their physiological targets using intracellular libraries as tools for chemical genetics in the HCV replicon (aim 4). The integrated technology that will emerge from...

**7/3,K/13 (Item 1 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0347051 DBR Accession No.: 2004-19343 PATENT
**Novel isolated polypeptide having ability to bind to kinase domain region or vascular endothelial growth factor/kinase domain region complex, useful in *inhibiting* vascular endothelial growth factor activation of kinase domain region - involving vector-mediated gene transfer and expression in host cell**
AUTHOR: SATO A K; SEXTON D J; DRANSFIELD D T; LADNER R C; ARBOGAST C; BUSSAT P; FAN H; KHURANA S; LINDER K E; MARINELLI E R; NANJAPPAN P ; NUNN A; PILLAI R; POCHON S; RAMALINGAM K; SHRIVASTAVA A; SONG B ; SWENSON R E; VON WRONSKI M A
PATENT ASSIGNEE: DYAX CORP; BRACCO INT BV 2004
PATENT NUMBER: WO 200465621 PATENT DATE: 20040805 WPI ACCESSION NO.: 2004-580734 (200456)
PRIORITY APPLIC. NO.: WO 20036731 APPLIC. DATE: 20030303
NATIONAL APPLIC. NO.: WO 2003US28787 APPLIC. DATE: 20030911
LANGUAGE: English

**Novel isolated polypeptide having ability to bind to kinase domain region or vascular endothelial growth factor/kinase domain region complex, useful in *inhibiting* vascular endothelial growth factor activation of kinase domain region - involving vector-mediated gene transfer and expression in host cell**
...ABSTRACT: in radiotherapy; (15) synthesizing (M4) a polypeptide or a multimeric polypeptide construct having the ability to bind KDR or VEGF/KDR complex, involves forming a *cyclic* *polypeptide* by introducing an amide bond between two side chains; (16) medical imaging using (I); (17) synthesizing a multimeric polypeptide construct having the ability to bind...

... ability to bind to KDR or VEGF/KDR, where each peptide of the dimer comprises a sequence chosen from any one of (S1)-(S12); (20) *inhibiting* VEGF-induced vascular permeability, involves administering an agent comprising (I); (21) a method for detecting KDR or VEGF/KDR complex in an animal or human...

... with (I) to form a complex with the KDR or VEGF/KDR complex target. ACTIVITY - Cytostatic; Antiangiogenic; Antimalarial; Anti-HIV; Virucide; Antibacterial. MECHANISM OF ACTION - *Inhibitor* of VEGF activation of KDR (claimed). No relevant biological data given. USE - (I) is useful for detecting KDR or VEGF/KDR complex in an animal...

... the labeled MPC to the subject, and detecting the labeled MPC in the subject, and optionally, constructing an image. (I) or MPC is useful for *inhibiting* angiogenesis, which involves administering to an animal or human subject, in need of treatment for such a condition, (I) or one or more of MPC, where the polypeptide comprises any one of (S1)-(S12). (I) or MPC is useful for *inhibiting* VEGF activation of KDR, which involves administering to an animal or human subject, in need of treatment for such a condition, (I) or MPC, where...

... by systemical, local, topical, intravenous, intramuscular, intraperitoneal, subcutaneous, gastrointestinal, transdermal, intravaginal or transalveolar route, at a dosage of 0.1 mug/kg-1 mg/kg. *ADVANTAGE* - (I) enables efficient detection, imaging and localization of activated endothelial cells exhibiting upregulated KDR expression and binding to VEGF. (I) enables improvement in the activity...

... resin-bound peptide was treated with 35% piperidine to remove Fmoc protecting group. Finally, after treating the peptides with dimethyl sulfoxide (DMSO) and water, crude *cyclic* disulfide containing *peptide* was obtained. The peptide was purified and was subjected to biotinylation, and labeled with 5-carboxyfluorescein. The prepared peptide was found to comprise sequences such...

**7/3,K/14 (Item 2 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0346161 DBR Accession No.: 2004-18453 PATENT
**Use of cyclin D1 *inhibitors* in the manufacture of a pharmaceutical preparation to improve therapeutic responses to anti-estrogen treatment of breast cancer - for use in cancer diagnosis and therapy**
AUTHOR: KRONBLAD A; STENDAHL M; LANDBERG G
PATENT ASSIGNEE: FORSKARPATENT I SYD AB 2004
PATENT NUMBER: WO 200462654 PATENT DATE: 20040729 WPI ACCESSION NO.: 2004-561752 (200454)
PRIORITY APPLIC. NO.: SE 200398 APPLIC. DATE: 20030115
NATIONAL APPLIC. NO.: WO 2004SE6 APPLIC. DATE: 20040109
LANGUAGE: English

**Use of cyclin D1 *inhibitors* in the manufacture of a pharmaceutical preparation to improve therapeutic responses to anti-estrogen treatment of breast cancer - for use in cancer diagnosis and therapy**
ABSTRACT: DERWENT ABSTRACT: NOVELTY - In the manufacture of a pharmaceutical preparation at least one cyclin D1 *inhibitor* (e.g. monoterpene, noridhydroguaiaretic acid, acyclic retinoid, sesquicillin) is used. DETAILED DESCRIPTION - In the manufacture of a pharmaceutical preparation to improve patients responses to anti-estrogen treatment following a breast cancer treatment, either surgical, using cytotoxic compounds and/or irradiation, at least one cyclin D1 *inhibitor* is used. The cyclic D1 *inhibitor* is selected from monoterpene, nordihydroguaiaretic acid, acyclic retinoid (ACR), sesquicillin, sulindac (NSAID), methylglyoxal-bis(cyclopentylamidinohydrazone), ANXA-1, FR-901228 (a *cyclic* *peptide* *inhibitor* of histone deacetylase), simvastatin (mevalonate/protein prenylation *inhibitor*), cerivastatin (*inhibitor* of hydroxymethylglutaryl-coenzyme A reductase), (-)-enantiomer of glossypol (polyphenolic pigment present in cottonseed), ursolic acid (pentacyclictriterpenoid), 14-epi-analogues of 1,25-dihydroxyvitamin D3, tangeritin (5,6,7,8,4'-pentamethoxyflavone), purvalanol A (protein kinase *inhibitor* ), tetrandrine, deoxybouvardin, lycopene, podophyllotoxin GL331, resveratrol, silymarin, epigallocatechin-3-gallate (EGCCG), piceatannol, exisulind, oxamflatin, androstanes or androstenes. ACTIVITY - Cytostatic. MECHANISM OF ACTION - Cyclin D1 *inhibitor*. USE - Cyclin D1 *inhibitors* are useful in the manufacture of a pharmaceutical preparation for treating anti-estrogen (e.g. tamoxifen) non-responsive breast cancer (claimed). *ADVANTAGE* - The cyclin D1 *inhibitors* improve response of cancer patients to anti-estrogen treatment; and subsequent patient survival. (18 pages)
DESCRIPTORS: cyclin-D1-*inhibitor*, monoterpene, noridhydroguaiaretic acid, acyclic retinoid, sesquicillin prep.; appl. mamma cancer diagnosis, therapy terpene tumor cytostatic (23, 38)

**7/3,K/15 (Item 3 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0345122 DBR Accession No.: 2004-17414 PATENT
**New peptide comprising a cyclic amino acid sequence of four to ten alternating D- and L-alpha amino acids useful for treating fungal infections - involving vector-mediated gene transfer and expression in host cel for use in therapy**

AUTHOR: SANCHEZ-QUESADA J; CABEZAS E
PATENT ASSIGNEE: ADAPTIVE THERAPEUTICS INC; WEINBERGER D; SANCHEZ-QUESADA J; CABEZAS E 2004
PATENT NUMBER: WO 200450685 PATENT DATE: 20040617 WPI ACCESSION NO.: 2004-487528 (200446)
PRIORITY APPLIC. NO.: US 429923 APPLIC. DATE: 20021129
NATIONAL APPLIC. NO.: WO 2003US38595 APPLIC. DATE: 20031126
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A *peptide* comprising a *cyclic* amino acid sequence of 4 - 10 (preferably 6 or 8) alternating D- and L-alpha amino acids (preferably polar, nonpolar and ionizable) is new. DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a pharmaceutical composition comprising a mixture of at least two *cyclic* *peptides* . ACTIVITY - Fungicide; Dermatological; Antiallergic; Respiratory-Gen.; Gastrointestinal-Gen.; Cardiovascular-Gen.; Uropathic; CNS-Gen.; Auditory. MECHANISM OF ACTION - Fungal cell death inducer. The antifungal activity of...

... candida vulvitis, candida balanitis and otitis extema and infections in immunocompromised patients (e.g. AIDS patients, patients receiving cancer therapy or transplant patients). ADMINISTRATION - The *cyclic* *peptide* applied to the nail (claimed). The peptides are administered in dosage of 0.01-750 (preferably 0.1-300, especially 1-20) mg/kg or...

... 0.1-2.5, especially 0.5-1) g/day orally, parenterally (including subcutaneously, intravenously, intramuscularly, or intraperitoneally), rectally, dermally, transdermally, intrathoracically, intrapulmonarily or intranasally. *ADVANTAGE* - The peptides possess antifungal activity without undesired anti-animal cell activity; have a minimum *inhibitory* concentration at which no target fungal organism grow in vitro is less than one twentieth to less than one half of the peptide concentration needed...

**7/3,K/16 (Item 4 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0328345 DBR Accession No.: 2004-00637 PATENT
**Antagonist that specifically binds denatured collagen but binds to native triple helical forms collagen with substantially reduced affinity, useful for *inhibiting* angiogenesis - monoclonal antibody preparation by hybridoma cell culture for protein triple helix binding and disease therapy**
AUTHOR: BROOKS P C; XU J; PETITCLERC E
PATENT ASSIGNEE: BROOKS P C; XU J; PETITCLERC E 2003
PATENT NUMBER: US 20030113331 PATENT DATE: 20030619 WPI ACCESSION NO.: 2003-810879 (200376)
PRIORITY APPLIC. NO.: US 478977 APPLIC. DATE: 20000106
NATIONAL APPLIC. NO.: US 478977 APPLIC. DATE: 20000106
LANGUAGE: English

**Antagonist that specifically binds denatured collagen but binds to native triple helical forms collagen with substantially reduced affinity, useful for *inhibiting* angiogenesis - monoclonal antibody preparation by hybridoma cell culture for protein triple helix binding and disease therapy**
...ABSTRACT: BIOTECHNOLOGY - Preferred Antagonist: In (I), the reduced affinity is about 3 fold, 5 fold or 10 fold lower than that for the denatured collagen. (I) *inhibits* angiogenesis. The denatured collagen is denatured collagen type-I, type-II, type-III, type-IV or type-V, preferably, denatured collagen type-I. The denatured...

... I) is a monoclonal antibody which has the binding specificity of monoclonal antibody HUI77, HUIV26 or XL313. (I) is a polyclonal antibody, polypeptide, a linear *peptide* or a *cyclic* *peptide*,

non-peptidic compound, oligonucleotide, humanized or chemically modified monoclonal antibody, or fragment of a monoclonal antibody. (I) is conjugated to cytotoxic or cytostatic agents. Preferred Method: In (M1), the putative antagonist is a non-peptidic compound, a polypeptide, linear *peptide* or a *cyclic* *peptide*, or an antibody. The non-peptidic compound is a small organic compound or oligonucleotide. The antibody is a monoclonal or polyclonal. The first and second...

... II) is Cys-Gln-Gly-Pro-Arg-Gly-Asp-Lys-Gly-Glu-Cys. ACTIVITY - Cytostatic; Ophthalmological; Vasotropic; Antipsoriatic; Antiinflammatory; Antiarthritic; Antirheumatic; Antidiabetic. MECHANISM OF ACTION - *Inhibitor* of angiogenesis. No biological data given. USE - (I) is useful for *inhibiting* angiogenesis in a tissue. (I) is administered in conjunction with chemotherapy or radiation. The tissue is inflamed and angiogenesis is occurring. The tissue is present in a mammal. The tissue is arthritic, ocular, retinal or hemangioma. (I) is useful for *inhibiting* tumor growth or metastasis, psoriasis, macular degeneration, or restenosis in a tissue. The tumor or metastasis is a melanoma, carcinoma, sarcoma, fibrosarcoma, glioma or astrocytoma...

... intravenous, transdermal, intrasynovial, intramuscular, intratummoral, intraocular, intranasal, intrathecal, topical or oral route (claimed). Dosage ranges from 0.1-300 (preferably 0.5-20) mg/kg. *ADVANTAGE* - (I) has potentially high specificity and has relatively low toxicity. EXAMPLE - Monoclonal antibody (Mab) HUI77 was generated and isolated by the immunological technique termed subtractive...

**7/3,K/17 (Item 5 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0326714 DBR Accession No.: 2003-27855 PATENT

**Novel cyclic-peptide compound or its salt, is useful in pharmaceuticals for preventing and treating circulatory diseases, such ischemic heart disease, angina, acute myocardial infarction and subarachnoid bleeding - cyclic peptide preparation by bacterium fermentation for disease therapy**

PATENT ASSIGNEE: YAMANOUCHI PHARM CO LTD 2003
PATENT NUMBER: JP 2003210190 PATENT DATE: 20030729 WPI ACCESSION NO.: 2003-783299 (200374)
PRIORITY APPLIC. NO.: JP 20029366 APPLIC. DATE: 20020118
NATIONAL APPLIC. NO.: JP 20029366 APPLIC. DATE: 20020118
LANGUAGE: Japanese

ABSTRACT: DERWENT ABSTRACT: NOVELTY - *Cyclic*-*peptide* compound (I) or its salt is new. DETAILED DESCRIPTION - *Cyclic*-*peptide* compound of formula (I) or its salt is new. R1 = hydrogen atom or group of formula (ii); R2-R4 = hydrogen atom; and R11 = methyl, ethyl...

... group substituted with hydrogen or halogen. INDEPENDENT CLAIMS are also included for: (1) preparation of (I); and (2) pharmaceuticals, which has (I) having platelet aggregation *inhibitory* effect, as active ingredient. ACTIVITY - Cardiant; Vasotropic; Antianginal; Thrombolytic; Anticoagulant; Cerebroprotective; Hemostatic. MECHANISM OF ACTION - Platelet Aggregation *Inhibitor* (claimed). Blood from healthy volunteers was mixed with sodium citrate, to obtain platelet rich plasma, by DeMarco's method described in J. Clin. Invest., 77...

...coronary-artery thrombolysis and subarachnoid bleeding. ADMINISTRATION - (I) is administered orally at a dose of 0.1-1000 (preferably 0.1-50) mg/adult/day. *ADVANTAGE* - The novel *cyclic* *peptide* compound is effectively utilized as platelet aggregation *inhibitor* in pharmaceuticals. EXAMPLE - The culture medium containing 1% glucose, 2% potato starch, 0.4% calcium carbonate, 0.5% polypeptone 0.5% yeast extract was sterilized...

... performed at 220 rpm at 28 degreesC. The culture product was further processed, fermented and finally passed through column chromatography, to obtain crystalline fraction of *cyclic* *peptide*. (17 pages)
DESCRIPTORS: platelet aggregation *inhibitor* cyclic peptide prep., Chromobacterium sp., culture medium evaluation, appl. thrombin receptor agonist pharmaceutical manufacture, circulatory disease, ischemic heart disease, angina, acute myocardial infarction, postoperative reobstruction...

**7/3,K/18 (Item 6 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0321171 DBR Accession No.: 2003-22311 PATENT
**Screening for cells having altered phenotype e.g. modulation of apoptosis, exocytosis, by selecting cells responsive to induction and repression of expression of nucleic acid sequence encoding candidate bioactive agent - retro virus vector-mediated gene transfer and expression in mammal cell for use in drug screening and disease gene therapy**
AUTHOR: LORENS J; KINSELLA T M; MASUDA E; HITOSHI Y; LIAO X C; PEARSALL D; FRIERA A; CHU P
PATENT ASSIGNEE: LORENS J; KINSELLA T M; MASUDA E; HITOSHI Y; LIAO X C; PEARSALL D; FRIERA A; CHU P 2003
PATENT NUMBER: US 20030022196 PATENT DATE: 20030130 WPI ACCESSION NO.: 2003-596331 (200356)
PRIORITY APPLIC. NO.: US 96339 APPLIC. DATE: 20020308
NATIONAL APPLIC. NO.: US 96339 APPLIC. DATE: 20020308
LANGUAGE: English

...ABSTRACT: M1) or (M2), the population of cells comprise a stimulator and the parent phenotype is due to the presence of the stimulator. (IV) is a *polypeptide* or *cyclic* *polypeptide*, an RNA, antisense RNA, or DNA. The first element is expressed in trans or in cis relative to (IV). (III) comprises a full-length cDNA...
...known proteins in cells, using the absence of normal cellular functions, the mammalian two hybrid system or fluorescence resonance energy transfer mechanisms for detection, etc. *ADVANTAGE* - The methods provide a significantly improvement over conventional screening techniques, by allowing rapid and highly efficient screening of large number of candidate bioactive agents in...

... response of cytokines like IL-4 and SOCS1 (suppressor of cytokine signaling). In the BH1-4 or BH2-A5 cell lines, SOCS1 and STAT6delta each *inhibited* the IL-4 inducible expression of HEBGF. The following five different retroviral vectors were constructed as positive controls for the screening assay, and the encoded...

... cells 6 days post infection for each of the five retroviral vectors, indicated that the expression of SOCS1-ires-GFP and GFP-SOCS1 retroviral constructs *inhibited* IL-4 signaling/induced expression of HBEGF. Further, the results indicated that the GFP report protein was an effective marker for monitoring SOCS1 expression in the screening assays. Finally, these results indicated that the expression of GFP-STAT6DELTA only partially *inhibited* IL-4 signaling/induced expression of HBEGF. (96 pages)

**7/3,K/19 (Item 7 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0318458 DBR Accession No.: 2003-19598 PATENT
**New peptides and related expression vectors, useful for *inhibiting* tumors, especially where caused by human papilloma virus, bind to the phosphorylation site of casein kinase II - recombinant fusion protein**

**for use in cancer and virus infection therapy**
AUTHOR: PEREA RODRIGUEZ S E; REYES ACOSTA O; SANTIAGO VISPO N F; PUCHADES IZAGUIRRE Y; SILVA RODRIGUEZ R; MORO SORIA A; SANTOS SAVIO A; GONZALEZ LOPEZ L J; GONZALEZ BARRIOS B
PATENT ASSIGNEE: CENT ING GENETICA and BIOTECNOLOGIA 2003
PATENT NUMBER: WO 200354002 PATENT DATE: 20030703 WPI ACCESSION NO.: 2003-514183 (200348)
PRIORITY APPLIC. NO.: CU 201U-000309 APPLIC. DATE: 20011220
NATIONAL APPLIC. NO.: WO 2002CU10 APPLIC. DATE: 20021204
LANGUAGE: Spanish

**New peptides and related expression vectors, useful for *inhibiting* tumors, especially where caused by human papilloma virus, bind to the phosphorylation site of casein kinase II - recombinant fusion protein for use in cancer and...**
...ABSTRACT: Gln-Cys. An INDEPENDENT CLAIM is also included for an expression vector, functional in mammalian cells, that contains a DNA sequence encoding (A). BIOTECHNOLOGY - Preferred *Peptides*: These are *cyclic* and may form part of a fusion peptide (synthetic or recombinant), e.g. to improve intracellular penetration, and then typical fusion partners are the Tat1...

... other day. After 30 days, the tumor volume was about 0.6 mm3 compared with 1.5 mm3 for untreated controls. MECHANISM OF ACTION - (A) *inhibit* casein kinase II and also bind to the phosphorylation site at positions 28-38 in the E7 oncoprotein of HPV, so are toxic to cervical carcinoma cells and also increase the sensitivity of such cells to interferon; Gene therapy. USE - (A) are used to *inhibit* growth of tumor cells, for treating cancers, particularly those caused by human papilloma virus (HPV), but also other tumors with high endogenous CKII activity, and...

... g. intraepithelial cervical neoplasia) caused by HPV. In addition vectors that contain a sequence encoding (A) are useful for gene therapy of HPV-associated cancers. *ADVANTAGE* - (A) are effective against HPV that are resistant to interferon, and since they target a highly conserved region of HPV should be effective against many...

**7/3,K/20 (Item 8 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0312188 DBR Accession No.: 2003-13328 PATENT
**New cyclic peptides useful for the treatment or prevention of e.g. obesity - anorectic and dermatological drug screening involving melanocortin-4 receptor gene transfer and expression in CHO cell culture**
AUTHOR: BEDNAREK M A
PATENT ASSIGNEE: MERCK and CO INC 2003
PATENT NUMBER: WO 200306604 PATENT DATE: 20030123 WPI ACCESSION NO.: 2003-300415 (200329)
PRIORITY APPLIC. NO.: US 304958 APPLIC. DATE: 20010712
NATIONAL APPLIC. NO.: WO 2002US21443 APPLIC. DATE: 20020708
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - *Cyclic* *peptides* (I) are new. DETAILED DESCRIPTION - *Cyclic* *peptides* of formula (I) or their salts are new. A = L-histidyl; B = L-arginyl; B1 = D-phenylalanyl (optionally para-substituted by F, Cl, Br, Me...

... serum albumin (1 mg/ml) to a concentration of 1 - 5x106 cells/ml. The cells were counted and the cell suspension was treated with phosphodiesterase *inhibitor* 3-isobutyl-1-methylxanthine. 9-(4-Chloro-benzyl)-6-(3-guanidino-propyl)-12-(1H-imidazol-4-ylmethyl)-3-(1H-indol-3-ylmethyl)-2,5,8...

... 1000 mg/day/kg orally, rectally, topically, parenterally (including

subcutaneously, intramuscularly or intravenously), ocularly (including ophthalmically), pulmonarily (nasally or through buccal inhalation), nasally or intranasally. *ADVANTAGE* - (I) are potent and selective agonists of the human melanocortin-4-receptor. Photoactive derivatives of (I) are made to incorporate an easily detectable group or...

**7/3,K/21 (Item 9 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0311616 DBR Accession No.: 2003-12756 PATENT
**Screened histone deacetylase *inhibitors* for remedies in treating prostate cancer and malignant lymphoma - drug screening, p21 and c-myc expression profiling for cancer therapy**
AUTHOR: SASAKAWA Y; NAOE Y
PATENT ASSIGNEE: FUJISAWA PHARM CO LTD 2003
PATENT NUMBER: WO 200315810 PATENT DATE: 20030227 WPI ACCESSION NO.: 2003-289940 (200328)
PRIORITY APPLIC. NO.: JP 2001250846 APPLIC. DATE: 20010821
NATIONAL APPLIC. NO.: WO 2002JP8355 APPLIC. DATE: 20020820
LANGUAGE: Japanese

**Screened histone deacetylase *inhibitors* for remedies in treating prostate cancer and malignant lymphoma - drug screening, p21 and c-myc expression profiling for cancer therapy**
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Remedies for prostate cancer, or malignant lymphoma except T cell lymphoma, contain a *cyclic* *tetrapeptide* (I) as active ingredient. DETAILED DESCRIPTION - Remedies for prostate cancer, or malignant lymphoma except T cell lymphoma, contain a *cyclic* *tetrapeptide* of formula (I) or its salt as active ingredient. INDEPENDENT CLAIMS are also included for; (1) drug compositions for treating prostate cancer, or malignant lymphoma ...

... of such drug compositions .in treating prostate cancer, or malignant lymphoma except T cell lymphoma; (5) a method for evaluating antitumor effect of histone deacetylase *inhibitors* comprising at least the treatment of test cells with *inhibitors*, and measuring changes in expression of a specific gene in the test cells before and after the treatment for comparison of the expression doses; or...

...a specific protein in the test cells before and after such treatment for comparison of the expression doses; (6) a method for screening histone deacetylase *inhibitors* that have site-specific antitumor activity by using the method for evaluation antitumor effect; and (7) a method for selecting genes by using the predicted...

...increases or decreased expression in the possible combinations. ACTIVITY - Cytostatic. MECHANISM OF ACTION - None given in source material. USE - The screened compounds are histone deacetylase *inhibitors* which can be used as remedies in treating prostate cancer and malignant lymphoma. ADMINISTRATION - Administration is oral or non-oral and dosage is e.g. 5-30 mg. *ADVANTAGE* - These screened compounds are applicable clinically in vitro and in vivo, with specificity in targeting tumor cells. EXAMPLE - A drug composition was formulated from FR901228...
DESCRIPTORS: histone-deacetylase-*inhibitor* cyclic tetrapeptide FR901228 comp., drug screening, p21, c-myc gene expression profiling, mouse evaluation, appl. prostate cancer, malignant lymphoma therapy enzyme-*inhibitor* oncoprotein mammal animal tumor (22, 21)

**7/3,K/22 (Item 10 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0309290 DBR Accession No.: 2003-11075 PATENT

**New cyclic polypeptides useful for preparation of a medicament for treatment of at least one symptom of e.g. Menieres disease - vector-mediated recombinant protein gene transfer and expression in host cell for use in cancer prevention and therapy**

AUTHOR: LARSEN B D; NEVE S; QVORTRUP K; PETERSEN J S; MEIER E
PATENT ASSIGNEE: ZEALAND PHARMA AS 2002
PATENT NUMBER: WO 200279235 PATENT DATE: 20021010 WPI ACCESSION NO.: 2003-221246 (200321)
PRIORITY APPLIC. NO.: DK 2001534 APPLIC. DATE: 20010330
NATIONAL APPLIC. NO.: WO 2002IB2466 APPLIC. DATE: 20020329
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - *Cyclic* *polypeptides* (c1) are new. (c1) is capable of *inhibiting* binding of guanylin or a compound, which comprises guanylin like activity to guanylin cyclase C. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following...

...epitope; (2) an antibody (a2) specifically binding to a guanylyl cyclase C epitope comprising the amino acid sequence of formula (S2); (3) use of an *inhibitor* (E1) of guanylyl cyclase C activity for the preparation of a medicament for the treatment of Meniere's disease or related symptoms such as tinnitus, vertigo and hearing loss; (4) a pharmaceutical composition comprising an *inhibitor* (I1) of binder of guanylin or a compound which comprises guanylin like activity to guanylyl cyclase C, and a carrier; (5) a compound comprising an *inhibitor* (I2), which is a polypeptide of the sequence (S3) or (S4); (6) use of (c1), (a1), (a2) or (I2) for preparation of a medicament; (7 ...

... A'11, A'13, Xaa and A'14 = amino acid. ACTIVITY - Auditory; Cytostatic; Hypertensive; Vasotropic; Diuretic; Natriuretic. No biological data is given. MECHANISM OF ACTION - *Inhibitor* of binding guanylin or it's analog to guanylyl cyclase C; Guanylin antagonist; Modulator of guanylyl cyclase signaling receptor (GC-C). USE - For preparation of...

... can be administered subcutaneously, intramuscularly, intravenously, intraperitoneally, rectally, intralipomateously, epidurally, intratracheally, vaginally, bucally, ocularly, directly into the brain, pulmonarily or topically. No dosage is given. *ADVANTAGE* - The *inhibitor* can associate with guanylyl cyclase C resulting in cessation of the catalysis of cGMP synthesis by guanylyl cyclase C and facilitates diuresis in a mammal...

**7/3,K/23 (Item 11 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0309214 DBR Accession No.: 2003-10999 PATENT
**Altering recombinant adeno-associated virus (rAAV) transduction of mammalian cell by contacting cell with pseudotyped rAAV having combination of AAV capsid protein and rAAV genome, and agent that alters virus transduction - recombinant adeno-associated virus vector-mediated gene transfer and expression in host cell for use in gene therapy**

AUTHOR: ENGELHARDT J F; YAN Z
PATENT ASSIGNEE: UNIV IOWA RES FOUND; ENGELHARDT J F; YAN Z 2003
PATENT NUMBER: WO 2003006616 PATENT DATE: 20030123 WPI ACCESSION NO.: 2003-229480 (200322)
PRIORITY APPLIC. NO.: US 305204 APPLIC. DATE: 20010713
NATIONAL APPLIC. NO.: WO 2002US21926 APPLIC. DATE: 20020712
LANGUAGE: English

...ABSTRACT: molecule is from a serotype of AAV that is different than the serotype of AAV for the AAV capsid protein; and the second rAAV (2) *inhibiting* or treating (M3) a condition associated with the absence of, or reduced or aberrant, expression of an endogenous gene product,

involves contacting a mammal at...

... transduction and at least one rAAV comprising a transgene encoding at least a portion of functional gene product for the corresponding endogeneous gene product to *inhibit* or treat the condition, the at least one rAAV comprises AAV capsid protein and a first recombinant DNA molecule as described in (M2); and (3... a functional peptide or polypeptide. The cell contacted with the rAAV, expresses a functional peptide or polypeptide, preferably a therapeutic peptide or polypeptide. The functional *polypeptide* is *cyclic* fibrosis transmembrane conductance receptor, beta-globin, gamma-globin, tyrosine hydroxylase, glucocerebrosidase, aryl sulfatase A, factor VIII, dystrophin or erythropoietin. The second DNA segment of the...

... chimeric genome. The open reading frame encodes the functional peptide or polypeptide as described above. The agent preferably enhances viral transduction, and is a proteosome *inhibitor*. The agent *inhibits* the activation of ubiquitin, the transfer of ubiquitin to the ubiquitin carrier protein, ubiquitin ligase, or their combinations, preferably *inhibits* ubiquitin ligase. (M1) further involves administering a second agent that enhances the activity of the agent that alters transduction. Preferably the second agent is EGTA...

... cell. (M2) is useful for expressing functional peptide or polypeptide, preferably a therapeutic peptide or polypeptide, in a host cell as described above. The functional *polypeptide* is *cyclic* fibrosis transmembrane conductance receptor, beta-globin, gamma-globin, tyrosine hydroxylase, glucocerebrosidase, aryl sulfatase A, factor VIII, dystrophin or erythropoietin. (M3) is useful for treating of *inhibiting* a condition associated with the absence of, or reduced or aberrant, expression of an endogenous gene product. (All claimed.) (M3) is useful for treating or *inhibiting* a condition such as sickle cell anemia, thalassemias, hemophilias, and Fanconi anemias, neurological disorders such as Alzheimer's disease and Parkinson's disease, and muscle...

... parenteral including rectal, transdermal, subcutaneous, intravenous, intramuscular, intraperitoneal routes, etc at dosages ranging from 0.01 micro-M-1 mM, preferably 1-40 micro-M. *ADVANTAGE* - The method overcomes the current size limitation for transgenes within rAAV vectors, and allows for the incorporation of a larger transcriptional regulatory region, e.g... p40 promoter driving AAV-5 Cap expression. Transduction efficiencies of rAAV-2RSVluc and rAAV-2cap5RSVluc were compared in the presence or absence of tripeptyl proteosome *inhibitors* (40 micro-M N-acetyl-L-Leucyl-L-Leucyl-norleucine (LLnL) or 4 micro-M carbobenzoxy-L-Leucyl-L-Leucyl-L-leucinal (ZLL, also referred...

... demonstrated augmentation of both rAAV-2 or rAAV-2cap5 transduction in the presence of LLnL or ZLL. No significant differences in the effect of these *inhibitors* on the transduction of native and pseudotyped viruses were found for fetal fibroblasts and 293 cells. However, a significantly higher induction of transgene expression was...

**7/3,K/24 (Item 12 from file: 357)**

DIALOG(R)File 357:Derwent Biotech Res.


0307207 DBR Accession No.: 2003-08992 PATENT

**New cyclic peptide derivatives useful for the treatment of fungal infectious diseases - fungicide production from Phoma sp. for human and veterinary fungus infection therapy**

AUTHOR: YANO T; INUKAI M; TAKATSU T; TANAKA I
PATENT ASSIGNEE: SANKYO CO LTD 2002
PATENT NUMBER: US 20020160946 PATENT DATE: 20021031 WPI ACCESSION NO.: 2003-182735 (200318)
PRIORITY APPLIC. NO.: JP 200252496 APPLIC. DATE: 20020228

NATIONAL APPLIC. NO.: US 87633 APPLIC. DATE: 20020301
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - *Cyclic* *peptide* derivatives are new. DETAILED DESCRIPTION - *Cyclic* *peptide* derivatives selected from 3-methyl-2-methylamino-pentanoic acid (8-sec-butyl-14-(1-hydroxy-ethyl)-5,11,23-triisobutyl-2,17-diisopropyl-10,16...

...cyclooctacos-27-yl)-amide are new. An INDEPENDENT CLAIM is also included for preparation of (I) and (II). ACTIVITY - Fungicide. MECHANISM OF ACTION - Fungal growth *inhibitor*. 3-Methyl-2-methylamino-pentanoic acid (8-sec-butyl-14-(1-hydroxy-ethyl)-5,11,23-triisobutyl-2,17-diisopropyl-10,16,20,22,26...

...nonaoxo-1,4,25- trioxa-7,10,13,16,19,22-hexaaza-cyclooctacos-27-yl)-amide (F-15078A) was tested for its fungicidal activity. Minimum *inhibitory* concentration (MIC) was determined by broth dilution method according to Yamaguchi, H., et al.; J, Med. Mycol. 36, 61 (1995) on a microtiter plate with...

... preferably 0.01-200, especially 0.1-20) mg per day for an adult human orally or parenterally (including intravenously, intramuscularly, subcutaneously, intracutaneously or intraperitoneally). *ADVANTAGE* - (I) exhibits fungicidal activity. EXAMPLE - A previously grown seed of Phoma sp. strain SANK 13899 was inoculated into previously sterilized preseed culture medium (300 l...

**7/3,K/25 (Item 13 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0297706 DBR Accession No.: 2002-19553 PATENT
**New cyclic peptides are human platelet aggregation receptor GPIIb/IIIa binders used for treating thrombosis, stroke and vascular graft occlusion - receptor binding protein preparation for disease therapy**
AUTHOR: PIERSCHBACHER M D; LUKEMAN D S; CHENG S; CRAIG W S; TSCHOPP J F
PATENT ASSIGNEE: LA JOLLA CANCER RES FOUND 2002
PATENT NUMBER: US 6395873 PATENT DATE: 20020528 WPI ACCESSION NO.: 2002-565129 (200260)
PRIORITY APPLIC. NO.: US 456466 APPLIC. DATE: 19950601
NATIONAL APPLIC. NO.: US 456466 APPLIC. DATE: 19950601
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - *Cyclic* *peptides* (I) are new. DETAILED DESCRIPTION - *Cyclic* *peptides* of formula X1X2X3X4GDX5X6X7 (I) are new. X2, X6 = groups linked by a bridge; X3 = 1-10 amino acid residues; X1, X7 = 0-20 amino acid...

... caused by undesirable platelet aggregation including thrombosis, stroke and vascular graft occlusion. ADMINISTRATION - The dosage is 1-50 mg/kg/hour, by infusion or injection. *ADVANTAGE* - (I) *Inhibit* platelet aggregation without causing prolonged bleeding time. (I) Have high affinity for the receptor IIb/IIIa and a low affinity for the fibronectin and vitronectin receptors. (I) Prevent inappropriate growth of vascular smooth muscle cells and arterial graft occlusion. (I) *Inhibit* the binding of fibrinogen to GPIIb/IIIa more than the binding of van Willebrand factor to GPIIb/IIIa. EXAMPLE - Peptides of sequence Ac-CNPRGD(Y...

...5) and eluted with a gradient of buffer B consisting of 60% acetonitrile and 40% buffer A. Eluted fractions were tested for their ability to *inhibit* receptor binding. The major peak obtained from the C18 column constituted 90% of recovered peptide and was deduced to be a monomeric, *cyclic* *peptide* because it was retained on the column for the length of time predicted for that sequence and because the uncyclized material multimeric forms were well...

**7/3,K/26 (Item 14 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0285664 DBR Accession No.: 2002-07511 PATENT
**New synthetic peptides mimicking beneficial trophic and neuritogenic effects of fibroblast growth factor, useful for stimulating neurite outgrowth and cell survival and treating prion disease and multiple sclerosis - recombinant protein production in cell culture useful for neurite outgrowth stimulator, cell survival stimulator, angiogenesis modulator and gene therapy**
AUTHOR: SAFFELL J L
PATENT ASSIGNEE: IMPERIAL COLLEGE INNOVATIONS LTD; KINGS COLLEGE LONDON 2001
PATENT NUMBER: WO 200196364 PATENT DATE: 20011220 WPI ACCESSION NO.: 2002-098050 (200213)
PRIORITY APPLIC. NO.: GB 200014870 APPLIC. DATE: 20000616
NATIONAL APPLIC. NO.: WO 2001GB2660 APPLIC. DATE: 20010618
LANGUAGE: English

...ABSTRACT: at the N-terminus and/or an amide group at the carboxy terminus. (I) comprises two cysteine residues that form a disulfide bond giving a *cyclic* *peptide*. The amino acids at positions 2 and 3 in (S1) are natural amino acids, non-natural amino acids, or modified amino acids. The amino acids...
... for topical administration. ACTIVITY - Neuroprotective; nootropic; antiparkinsonian; antidiabetic; vulnerary; vasotropic; antitumor. MECHANISM OF ACTION - Neurite outgrowth stimulator; cell survival stimulator; angiogenesis modulator; gene therapy; FGF *inhibitor*. The ability of the peptides to stimulate neurite outgrowth (axon regeneration) can be tested in a neurite outgrowth assay in vitro. Monolayers of NIH 3T3...paralysis caused by spinal cord injuries) after trauma or surgery in humans; stimulating angiogenesis in cardiac muscle; treating ischemia e.g., ischemia caused by stroke; *inhibiting* or reducing angiogenesis in a tumor in humans. (I)-(III) is used as a medicament for the above mentioned conditions, or for manufacturing the medicament...

... any pathological conditions for which FGF is used, and the peptides may also be used to promote wound healing. The peptides are also useful for *inhibiting* an undesirable effect of FGF by blocking FGF binding to its receptor without stimulating the receptor. ADMINISTRATION - The peptides or nucleic acids encoding them are...

... range from 20-500 microgram/kg body weight. Suitable dosage of peptides for intranasal administration range from 0.01 pg-1 mg/kg body weight. *ADVANTAGE* - (I)-(III) mimic the beneficial trophic and neuritogenic effects of FGF of high affinity receptor activation but lack the undesirable mitogenic and apoptotic effects of...

... diisopropylethylamine after removal of the N-alpha-t-butoxycarbonyl by acidolysis using trifluoroacetic acid. Peptide dendrimers (multiple antigenic peptides, MAP) were prepared by standard procedures. *Cyclic* *peptides* may be produced by synthesizing linear peptides synthesized as described above with a cysteine residue flanking each end of the peptide sequence. The cysteine was...

**7/3,K/27 (Item 15 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0283756 DBR Accession No.: 2002-05603 PATENT
**Novel non-naturally occurring nucleic acid (RNA) ligand to a beta-3 type integrin, useful in the treatment of cancer and thrombosis - RNA ligand**

**preparation and purification by Systematic Evolution of Ligands by EXponential Enrichment and antibody, DNA library, DNA primer and reverse transcription-polymerase chain reaction for genetherapy**

AUTHOR: RUCKMAN J; GOLD L; STEPHENS A; JANJIC N
PATENT ASSIGNEE: GILEAD SCI INC 2001
PATENT NUMBER: US 6331394 PATENT DATE: 20011218 WPI ACCESSION NO.: 2002-121160 (200216)
PRIORITY APPLIC. NO.: US 606477 APPLIC. DATE: 20000629
NATIONAL APPLIC. NO.: US 364543 APPLIC. DATE: 19990729
LANGUAGE: English

...ABSTRACT: acids. ACTIVITY - Cytostatic; thrombolytic; cardiant; antidiabetic; ophthalmological; antipsoriatic; gynecological. No supporting data given. MECHANISM OF ACTION - Nucleic acid ligand for integrins; alphaIIbbeta3 and alphavbeta3 binding *inhibitor*. To test whether aptamer 17.16 (a fully defined 84 RNA sequence given in the specification) could block the ligand binding site of alphaIIbbeta3 and ...

... concentration of biotinylated ligand (fibrinogen: 6 nM final; vitronectin: 10 nM final) was pre-mixed in binding buffer with varying concentrations of aptamer, control RNA, *cyclic* RGD *peptide*, antibody, or unmodified ligand. The mixtures were incubated in the integrin-coated wells for 60 minutes at room temperature. After washing, bound biotinylated ligand was...

...exclusive binding of two ligands to a single target species (Gill et al. (1991) J. Mol. Biol. 220:307-24). The concentration of competitor that *inhibited* 50% of the maximum signal above background (IC50) was determined from the fitted curve. Known ligand binding *inhibitors*, including an RGD peptide and the alphavbeta3-specific antibody LM609, were included as positive controls for the assay. Aptamer 17.16 *inhibited* the binding interaction with an IC50 of 4.7 nM while the control RNA showed no *inhibition*. By comparison, the IC50 of RGD peptide *inhibition* was 1.4 nM and that of LM609 was 2.7 nM. Unmodified vitronectin *inhibited* the binding of the biotinylated material with an IC50 of 59 nM. Similar data were obtained for aptamer *inhibition* of fibrinogen binding to alphavbeta3 and for fibrinogen binding to alphaIIbbeta3. IC50 values for alphavbeta3 *inhibition* were 17.16, 9.5 nM; control RNA, not measurable; RGD peptide, 1.0 nM; LM609, 6.3 nM; unmodified fibrinogen, 43 nM. IC50 values for alphaIIbbeta3 *inhibition* were: 17.16, 6.5 nM; control RNA, not measurable; RGD peptide, 21 nM; unmodified fibrinogen, 15 nM. Aptamer 17.16 is an effective competitor of beta3 integrin ligand binding and, on a molar basis, has an *inhibitory* potency nearly equivalent to that of a bivalent antibody. USE - (I) is especially useful as an *inhibitor* of alphaIIbbeta3 and alphavbeta3 integrins and can be used to *inhibit* tumor growth and metastasis. They can also be used to treat ocular diseases including diabetic retinopathy, retinopathy of prematurity, and macular degeneration. Other diseases treated...

... is detected by radioimaging at a critical site in the body, then anticoagulant and thrombolytic treatment, including treatment with (I), can be given locally. The *advantage* of using (I) as an imaging agent is that the anticoagulant and thrombolytic treatments, which can cause harm if administered prophylactically by allowing internal bleeding... higher concentrations into the bloodstream in the hope that some active agent will be carried to all potential sites of thrombosis. ADMINISTRATION - No details given. *ADVANTAGE* - (I), because of its specificity for the active, ligand-binding conformation of the integrin alphaIIbbeta3, may reduce the risk of bleeding complications associated with the existing anti-clotting therapies. Given the role of integrins in various disease states, the availability of high specificity *inhibitors* of integrins such as (I) is a particular *advantage*. EXAMPLE - (I) was generated using the SELEX (Systematic Evolution of Ligands by EXponential Enrichment). A DNA template library of sequence (5'-ttatacgactcactatagggagacaagaataaacgctcaannnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnttcgacaggaggctcacaacaggc-3') , was...

... and washed 5 times in binding buffer. RNAs that remained bound to the beads were eluted overnight at 37degreesC in binding buffer plus 100 microM *cyclic* RGD *peptide* (cRGD). Eluted RNAs were extracted with phenol, then chloroform:isoamyl alcohol (24:1), and ethanol precipitated. The RNA pellet was resuspended and annealed to primer...

**7/3,K/28 (Item 16 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0283418 DBR Accession No.: 2002-05265 PATENT
**Ligand useful for modulating immune response such as in the preparation of vaccine comprises CD21 contacting amino acid residues of C3d molecule - involving vector-mediated gene transfer for expression in host cell**
AUTHOR: ISENMAN D E; CLEMENZA L
PATENT ASSIGNEE: UNIV TORONTO 2001
PATENT NUMBER: WO 200192295 PATENT DATE: 20011206 WPI ACCESSION NO.: 2002-114323 (200215)
PRIORITY APPLIC. NO.: US 207434 APPLIC. DATE: 20000530
NATIONAL APPLIC. NO.: WO 2001CA785 APPLIC. DATE: 20010530
LANGUAGE: English

...ABSTRACT: and (VI) a host cell comprising the expression vector. BIOTECHNOLOGY - Preferred Components: The ligand is a fragment of C3d, a peptide, a mimetic or a *cyclic* *peptide* mimetic (preferably *cyclic* *peptide* mimetic containing a disulfide bond). The analog has an amino acid sequence corresponding to the amino acid sequence of wild-type C3d in which at...

... as vaccine (preferably tumor vaccine) (claimed), and as antigens in immunogenic compositions, therapeutics diagnostic reagents, in the generation of diagnostic agents and as cancer therapeutics. *ADVANTAGE* - The ligand has the ability to bind CD21 and stimulate B cells through the CD21/CD19 complex. The non-naturally occurring ligand and the analog...

... human CD21 mAb, before the addition of iC3b-coated erythrocytes. The IgG2b anti-CR3 mAb OKMI was used as negative control of Ab binding. Rosette *inhibition* by purified iC3b and C3dg was performed as above for the OKB7 blocking mAb experiments except that instead of OKB7, the Raji cells were pre...

... purified iC3b or C3dg before the addition of EAC423bi cells made with purified C3, which showed approximately 80 - 90% rosette formation in the absence of *inhibitor*. C4 was used as a negative control in the experiments. (43 pages)

**7/3,K/29 (Item 1 from file: 156)**
DIALOG(R)File 156:ToxFile


00567398 NLM Doc No: CRISP/94/NS26511-05 Sec. Source ID: CRISP/94/NS26511-05
**MUSCARINIC RECEPTOR COUPLING MECHANISMS IN THE BRAIN**
EHLERT FJ
UNIVERSITY OF CALIFORNIA, COLLEGE OF MEDICINE, IRVINE, CA 92717
Source: Crisp Data Base National Institutes Of Health
City or State: CALIFORNIA Zip Code: 92717
Pub. Year: 1992
Sponsoring Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL INST OF NEUROLOGICAL DISORDERS AND STROKE
Award Type: Grant
Document type: Research

Languages: ENGLISH
Record type: Completed

... phosphorylation of adenylate cyclase by protein kinase C. Consequently, the ability of muscarinic agonists to potentiate or modulate the effects which other neurotransmitters, drugs and *peptides* have on *cyclic* AMP accumulation in a variety of intact cell preparations from brain and peripheral tissues will be investigated. The potentially confounding effect of direct *inhibition* of adenylate cyclase by muscarinic receptors via the *inhibitory* guanine nucleotide binding protein will be eliminated by first pretreating tissue with pertussis toxin or by taking *advantage* of differences in the coupling of subtypes of the muscarinic receptor to phosphoinositide hydrolysis and *inhibition* of adenylate cyclase. The pharmacological characteristics of the subtypes of the muscarinic receptor responsible for activation of phosphoinositide hydrolysis and *inhibition* of adenylate cyclase will be defined in identical preparations of the corpus striatum and parotid gland by using pharmacological null methods and radioligand binding methods...
?

PATENT ASSIGNEE(S): 3-Dimensional Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003095625 | A2 | 20031120 | WO 2003-US14923 | 20030513 |
| WO 2003095625 | A3 | 20040715 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-379617P P 20020513
OTHER SOURCE(S): MARPAT 140:776

AB The invention provides a method for protecting one or more cells from programmed cytotoxic cell death by contacting the cells with a cytoprotective amount of an **MDM2** and/or HDM2 inhibitor. The cytoprotective amount of inhibitor is typically used as a pulsed administration. Useful inhibitors include a class of 1,4-benzodiazepines which act as inhibitors of **MDM2-p53** interactions. The method of the invention can be employed as an adjunct to chemotherapy or radiation therapy. In addition, the methods of the invention can be employed to treat a disease or condition that involves excessive cell death.

IT **186180-20-1 393113-21-8**
RL: PRP (Properties)
(unclaimed protein sequence; method using benzodiazepine compds. for cytoprotection through **MDM2** and HDM2 inhibition)

L18 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:818235 HCAPLUS
DOCUMENT NUMBER: 139:322283
TITLE: Methods for production and use of mammalian complementarity determining region mimetibodies for diagnosis and therapy of human diseases
INVENTOR(S): Heavner, George A.; Knight, David M.; Scallon, Bernard J.; Ghrayeb, John
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003084477 | A2 | 20031016 | WO 2003-US9139 | 20030324 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-368791P P 20020329

AB This invention pertains to methods for production and use of mammalian complementarity determining region (CDR) mimetibodies for diagnosis and therapy of human diseases. Genetic engineering, expression, and purification of human mimetibodies containing Ig fragments (CDR, variable, framework and/or constant region) as well as a ligand binding domain are disclosed in this invention. Peptides that mimic the activity of EPO, TPO, growth hormones, G-CSF, GM-CSF, IL-1ra, leptin, CTLA4, TRAIL, TGF-α and TGF-β are the focus of this genetic engineering. The aim of the invention is use of the purified recombinant proteins for diagnosis or treatment of anemia, immune or autoimmune disease, cancer, or infectious diseases. At the time of publication, claimed sequence nos. 997 to 1109 were missing, and claimed sequence nos. 984 to 996 were not clearly identified.

IT **186180-20-1 186180-21-2 186180-22-3**
**186180-23-4 186180-24-5 186180-25-6**
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Mdm**/hdm antagonist peptide; methods for production and use of mammalian CDR mimetibodies for diagnosis and therapy of human diseases)

L18 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:545267 HCAPLUS
DOCUMENT NUMBER: 139:226753
TITLE: Mixed-element capture agents: A simple strategy for the construction of synthetic, high-affinity protein capture ligands
AUTHOR(S): Bachhawat-Sikder, Kiran; Kodadek, Thomas
CORPORATE SOURCE: Center for Biomedical Inventions and the Departments of Internal Medicine and Molecular Biology, University of Texas Southwestern Medical Center, Dallas, TX, 75390-8573, USA
SOURCE: Journal of the American Chemical Society (2003), 125(32), 9550-9551
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Demonstration of a simple strategy to generate synthetic high-affinity protein capture agents of practical utility for protein-detecting microarrays. The model study highlights capture of the MBP-**Mdm2** fusion protein on a solid support by a linear sequence of peptides that bind to the two individual polypeptide chains.

IT **595567-95-6**
RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
(construction of synthetic, high-affinity protein capture ligands)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:509384 HCAPLUS
DOCUMENT NUMBER: 140:52744
TITLE: An interesting approach for cancer therapy: inhibition of the association of human double minute 2 with tumor suppressor **p53**
AUTHOR(S): **Garcia-Echeverria, Carlos; Chene, Patrick**; Blommers, Marcel J. J.; **Furet, P.**
CORPORATE SOURCE: Oncology Research, Novartis Pharma Inc., Basel, CH-4002, Switz.
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 53-54. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB As part of our drug discovery program to identify low mol. weight inhibitors of the association of hdm2 with **p53**, we have attempted to determine the amino acid specificities of the binding pockets of hdm2 in order to establish a pharmacophore model for this protein-protein interaction. This work has resulted in the identification of a highly potent peptide inhibitor of the **p53**/hdm2 protein-protein interaction.
IT **201984-21-6**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(low mol. wt inhibitors of the association of human double minute 2 with tumor suppressor **p53** as potential cancer therapy)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:829830 HCAPLUS
DOCUMENT NUMBER: 136:128583
TITLE: QSAR: hydropathic analysis of inhibitors of the **p53-mdm2** interaction
AUTHOR(S): Galatin, Peter S.; Abraham, Donald J.
CORPORATE SOURCE: Department of Medicinal Chemistry and Institute for Structural Biology and Drug Discovery, Virginia Commonwealth University, Richmond, VA, 23298, USA
SOURCE: Proteins: Structure, Function, and Genetics (2001), 45(3), 169-175
CODEN: PSFGEY; ISSN: 0887-3585
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To date, a number of **p53**-derived peptides have been evaluated in vitro for their ability to inhibit the carcinogenic **p53-mdm2** interaction. Design of second-generation nonpeptidic compds. requires the reduction of large peptide structures down to small mols. maintaining the proper spatial arrangement of key functional groups. Mol. modeling software exists that can predict and rank intermol. interactions from the **p53-mdm2** complex crystal structure. Such analyses can yield a pharmacophore model suitable as a search query for a 3D chemical database to generate new lead compds. As preliminary validation of this methodol., the Hydropathic INTeractions (HINT) program has been used to generate noncovalent interaction measurements between reported

peptide inhibitors and **mdm2**. Quant. structure-activity relationships were developed expressing peptide activity as a linear combination of hydropathic descriptors. In general, HINT measurements accurately modeled the effects of even single-atom alterations of the **p53**-peptide structure on activity, accounting for 70-90% of variation in exptl. inhibition consts. These results surpassed those of a recently described mol. dynamics-based approach and required significantly less computation time. In conclusion, the HINT program can be integrated into the drug design cycle for next-generation **p53-mdm2** complex inhibitors with confidence in its ability to simulate this noteworthy protein-protein interaction.

IT **393113-21-8 393113-23-0 393113-24-1 393113-25-2**
RL: PAC (Pharmacological activity); BIOL (Biological study) (QSAR hydropathic anal. of inhibitors of **p53-mdm2** interaction)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:537884 HCAPLUS
DOCUMENT NUMBER: 133:246812
TITLE: Discovery of Potent Antagonists of the Interaction between Human Double Minute 2 and Tumor Suppressor **p53**
AUTHOR(S): **Garcia-Echeverria, Carlos; Chene, Patrick**; Blommers, Marcel J. J.; **Furet, Pascal**
CORPORATE SOURCE: Oncology Research and Core Technologies, Novartis Pharma Inc., Basel, CH-4002, Switz.
SOURCE: Journal of Medicinal Chemistry (2000), 43(17), 3205-3208
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As part of a drug discovery program to identify antagonists of the **p53**/hdm2 (human double minute 2) protein-protein interaction, the authors have attempted to determine the amino acid specificities of hdm2's binding pockets to establish a pharmacophore model for this protein-protein interaction. This work has resulted in the identification of highly potent peptide antagonists. Structural information has been exploited to increase the hdm2-binding affinity of short peptide motifs derived from the N-terminal domain of the human wild-type **p53** protein. Combining conformational constraints as selected by mol. modeling with functional groups that are able to establish addnl. electrostatic and van der Waals interactions with the hdm2 protein, the authors have been able to increase the hdm2-binding affinity of the authors initial peptide 1700-fold. Particularly interesting is the increase in binding affinity obtained by replacing tryptophan with 6-chlorotryptophan (IC50 = 314 nM vs. IC50 = 5 nM, 63-fold). The new interactions identified and exptl. confirmed in this work could be directly applied to the optimization of nonpeptidic leads or incorporated into the "de novo" design of antagonists of the **p53**/hdm2 protein-protein interaction.

IT **201984-21-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(discovery of potent antagonists of interaction between human double minute 2 and tumor suppressor **p53**)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:291095 HCAPLUS
DOCUMENT NUMBER: 132:329919
TITLE: Modified peptides containing an antibody Fc domain as therapeutic agents
INVENTOR(S): Feige, Ulrich; Liu, Chuan-fa; Cheetham, Janet; Boone, Thomas Charles
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 608 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000024782 | A2 | 20000504 | WO 1999-US25044 | 19991025 |
| WO 2000024782 | A3 | 20020606 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6660843 | B1 | 20031209 | US 1999-428082 | 19991022 |
| EP 1144454 | A2 | 20011017 | EP 1999-971003 | 19991025 |
| EP 1144454 | A3 | 20020911 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9914708 | A | 20020716 | BR 1999-14708 | 19991025 |
| JP 2003512011 | T2 | 20030402 | JP 2000-578351 | 19991025 |
| AU 767725 | B2 | 20031120 | AU 2000-12322 | 19991025 |
| NZ 510888 | A | 20040130 | NZ 1999-510888 | 19991025 |
| ZA 2001002753 | A | 20020611 | ZA 2001-2753 | 20010404 |
| NO 2001001963 | A | 20010621 | NO 2001-1963 | 20010420 |
| BG 105461 | A | 20030430 | BG 2001-105461 | 20010424 |
| US 2004044188 | A1 | 20040304 | US 2003-609217 | 20030627 |
| US 2004053845 | A1 | 20040318 | US 2003-632388 | 20030731 |
| US 2004071712 | A1 | 20040415 | US 2003-645761 | 20030818 |
| US 2004057953 | A1 | 20040325 | US 2003-651723 | 20030829 |
| US 2004087778 | A1 | 20040506 | US 2003-653048 | 20030829 |
| US 2004077022 | A1 | 20040422 | US 2003-666696 | 20030919 |
| PRIORITY APPLN. INFO.: | | | US 1998-105371P | P 19981023 |
| | | | US 1999-428082 | A 19991022 |
| | | | WO 1999-US25044 | W 19991025 |
| | | | US 2000-563286 | A1 20000503 |

AB The present invention concerns fusion of Fc domains with biol. active peptides and a process for preparing pharmaceutical agents using biol. active peptides. In this invention, pharmacol. active compds. are prepared by a process comprising: (a) selecting at least one peptide that modulates the

activity of a protein of interest; and (b) preparing a pharmacol. agent comprising an Fc domain covalently linked to at least one amino acid of the selected peptide. Linkage to the vehicle increases the half-life of the peptide, which otherwise would be quickly degraded in vivo. The preferred vehicle is an Fc domain. The peptide is preferably selected by phage display, Escherichia coli coli display, ribosome display, RNA-peptide screening, or chemical-peptide screening.

IT **186180-20-1D**, fusion protein with IgG1 Fc domain
**186180-21-2D**, fusion protein with IgG1 Fc domain
**186180-22-3D**, fusion protein with IgG1 Fc domain
**186180-23-4D**, fusion protein with IgG1 Fc domain
**186180-24-5D**, fusion protein with IgG1 Fc domain
**186180-25-6D**, fusion protein with IgG1 Fc domain
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Mdm**/hdm antagonist; modified peptides containing an antibody Fc domain as therapeutic agents)

L18 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:241567 HCAPLUS
DOCUMENT NUMBER: 131:42875
TITLE: **p53** mediated death of cells overexpressing **MDM2** by an inhibitor of **MDM2** interaction with **p53**
AUTHOR(S): Wasylyk, Christine; Salvi, Roberto; Argentini, Manuela; Dureuil, Christine; Delumeau, Isabelle; Abecassis, Joseph; Debussche, Laurent; Wasylyk, Bohdan
CORPORATE SOURCE: Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, Illkirch, 67404, Fr.
SOURCE: Oncogene (1999), 18(11), 1921-1934
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **p53** tumor suppressor is frequently inactivated in human tumors. One form of inactivation results from overexpression of **MDM2**, that normally forms a neg. auto-regulatory loop with **p53** and inhibits its activity through complex formation. The authors have investigated whether disrupting the **MDM2**-**p53** complex in cells that overexpress **MDM2** is sufficient to trigger **p53** mediated cell death. The authors find that expression of a peptide homolog of **p53** that binds to **MDM2** leads to increased **p53** levels and transcriptional activity. The consequences are increased expression of the down-stream effectors **MDM2** and p21WAF1/CIP1, inhibition of colony formation, cell cycle arrest and cell death. There is also a decrease in E2F activity, that might have been due to the known phys. and functional interactions of **MDM2** with E2F1/DP1. However, this decrease is **p53** dependent, as are also colony formation, cell cycle arrest and cell death. These results show that a peptide homolog of **p53** is sufficient to induce **p53** dependent cell death in cells overexpressing **MDM2**, and support the notion that disruption of the **p53**-**MDM2** complex is a target for the development of therapeutic agents.

IT **186180-20-1 227200-18-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**p53**-**MDM2** inhibitor; **p53** mediated death of human osteosarcoma cells overexpressing **MDM2** by inhibitor

of **MDM2** interaction with **p53** in relation to)
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:709096 HCAPLUS
DOCUMENT NUMBER: 129:326112
TITLE: **Mdm2** binding domain conjugates for delivery of therapeutic and diagnostic substances to cells with inefficient **mdm2-p53** degradation pathway
INVENTOR(S): **Lane, David Philip**
PATENT ASSIGNEE(S): University of Dundee, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9847919 | A1 | 19981029 | WO 1998-GB1140 | 19980420 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9870642 | A1 | 19981113 | AU 1998-70642 | 19980420 |
| PRIORITY APPLN. INFO.: | | | GB 1997-8089 | 19970422 |
| | | | WO 1998-GB1140 | 19980420 |

AB **Mdm2** binds to **p53** in cells in which **mdm2** is not overexpressed, i.e. in cells in which **mdm2** is expressed at normal or low levels, and this interaction targets **p53** for degradation The invention exploits this mechanism of **p53** degradation to stabilize a substance comprising a **mdm2** binding domain linked to a coupling partner in cells in which this **mdm2** mediated degradation pathway does not operate efficiently. In contrast, in normal cells expressing functional **mdm2**, the substance will tend to be unstable as it will be marked for degradation through the interaction of the endogenous **mdm2** with the **mdm2** binding domain of the substance. Accordingly, the substances can be used to deliver the coupling partner to such cells, e.g. for use in the diagnosis and/or treatment of cancer, viral infections or other conditions associated with non functional **p53** or **mdm2**.
IT **215295-80-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TIP (thioredoxin insert protein) 12/1 peptide; **mdm2** binding domain conjugates for delivery of therapeutic and diagnostic substances to cells with inefficient **mdm2-p53** degradation pathway)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:708953 HCAPLUS
DOCUMENT NUMBER: 129:326111

TITLE: Materials and methods relating to inhibiting the interaction of **p53** and **mdm2**, and use for treatment of cancer, viral infections, or other conditions

INVENTOR(S): **Lane, David Philip**

PATENT ASSIGNEE(S): University of Dundee, UK

SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9847525 | A1 | 19981029 | WO 1998-GB1144 | 19980420 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9870644 | A1 | 19981113 | AU 1998-70644 | 19980420 |
| AU 731431 | B2 | 20010329 | | |
| EP 977580 | A1 | 20000209 | EP 1998-917411 | 19980420 |
| EP 977580 | B1 | 20030409 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 236651 | E | 20030415 | AT 1998-917411 | 19980420 |

PRIORITY APPLN. INFO.: GB 1997-8092 A 19970422
WO 1998-GB1144 W 19980420

AB **Mdm2** binds to **p53** in cells in which **mdm2** is not overexpressed, i.e. in cells in which **mdm2** is expressed at normal or low levels, and that in these cells, this interaction targets the **p53** for degradation This finding means that inhibiting **mdm2** production and/or inhibiting the binding of **mdm2** to **p53** allows levels of **p53** to increase by reducing the clearance of **p53** by **mdm2**, and can be used to activate **p53** function in cells other than those in which **mdm2** is overexpressed. This allows the use of an agent having the property of disrupting the binding of **p53** and **mdm2** or inhibiting the production of **mdm2** in a population of cells, in the preparation of a medicament for activating **p53**, wherein the population of cells do not overexpress **mdm2**. Such medicaments are useful in the treatment of conditions such as cancer, viral infections or conditions in which **p53** or **mdm2** is not functional. Peptide aptamer inserts into thioredoxin created potent inhibitors of the **p53**-**mdm2** interaction.

IT **215295-80-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide aptamer insert TIP 12/1; agents and methods for inhibiting **p53-mdm2** interaction, and use for treatment of cancer, viral infections, or other conditions, and screening method)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:65923 HCAPLUS
DOCUMENT NUMBER: 128:128291
TITLE: Preparation of compounds (peptides) capable of binding to **MDM2** for inhibition of the binding of **MDM2** to **p53** protein
INVENTOR(S): **Lane, David; Bottger, Volker; Bottger, Angelika; Picksley, Stephen ; Hochkeppel, Heinz-Kurt; Garcia-Echeverria, Carlos; Chene, Patrick; Furet, Pascal**
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Cancer Research Campaign Technology Ltd.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9801467 | A2 | 19980115 | WO 1997-EP3549 | 19970704 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2259149 | AA | 19980115 | CA 1997-2259149 | 19970704 |
| AU 9738479 | A1 | 19980202 | AU 1997-38479 | 19970704 |
| EP 958305 | A2 | 19991124 | EP 1997-935511 | 19970704 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO | | | | |
| NZ 333609 | A | 20000825 | NZ 1997-333609 | 19970704 |
| JP 2001500365 | T2 | 20010116 | JP 1998-504775 | 19970704 |
| US 2001018511 | A1 | 20010830 | US 1999-214371 | 19990326 |

PRIORITY APPLN. INFO.:
GB 1996-14197 A 19960705
GB 1997-7041 A 19970407
WO 1997-EP3549 W 19970704

OTHER SOURCE(S): MARPAT 128:128291

AB The present invention relates to compds. capable of binding to the oncogene protein **MDM2**, processes for the preparation of such compds., pharmaceutical prepns. comprising such compds., and uses of said compds., e.g. in the therapeutic (including prophylactic) treatment of an animal or especially of the human body (no data given). The title compds. R1XFXR2R3WXXR4 (R1 = Pro, Leu, Glu, Cys, Gln; X = natural amino acid; F = Phe; R2 = Arg, His, Glu, Cys, Ser, preferably Asp; R3 = His, Phe, preferably Tyr; W = Trp; R4 = Phe, Gln, preferably Leu) and their derivs. were prepared on Milligen 9050 automated peptide synthesizer by using the standard Boc and Fmoc chemical

IT **201984-20-5P 201984-22-7P 201984-39-6P**
**201984-41-0P 201984-43-2P 201984-45-4P**
**201984-47-6P 201984-49-8P 201984-68-1P**
**201984-97-6P 202075-45-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as inhibitors of the binding interaction between **MDM2** and protein **p53**)

L18 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:752178 HCAPLUS
DOCUMENT NUMBER: 126:112803
TITLE: Identification of novel **mdm2** binding peptides by phage display
AUTHOR(S): **Bottger, Volker; Bottger, Angelika**; Howard, Stephanie F.; **Picksley, Steven M.; Chene, Patrick; Garcia-Echeverria, Carlos; Hochkeppel, Heinz-Kurt; Lane, Daivd P.**
CORPORATE SOURCE: Cancer Res. Campaign Lab., Univ. Dundee, Dundee, DD1 4HN, UK
SOURCE: Oncogene (1996), 13(10), 2141-2147
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The oncogene **mdm2** and its human homolog hdm2 bind to the tumor suppressor protein **p53** and inactivate its function as a transcription factor. This has been implied as a possible mechanism for cancer development in several tumors including human sarcomas. The **mdm2-p53** interaction is therefore a much persued target for the development of anti-cancer drugs. In order to find novel high affinity ligands for hdm2 which would interfere with its binding to **p53** we screened phage display peptide libraries for **mdm2** binding phage. We found a series of 12 and 15mer peptides which interact strongly with hdm2. The peptide sequences show striking homol. with the previously established **mdm2** binding site on **p53**, confirming that the peptide defined 18TFSDLW23 region is crucial for the interaction but that contact between the two mols. extends to position L26 on **p53**. Free synthetic peptides derived from the phage selected sequences proved to be up to 100 times stronger inhibitors of the **p53-mdm2** interaction than the **p53** derived wt-peptide in several ELISA-assays. This illustrates the potency of phage display libraries in the search for new peptide based lead structures designed to mimic or inhibit therapeutically important protein-protein interactions.

IT **186180-20-1P 186180-21-2P 186180-22-3P**
**186180-23-4P 186180-24-5P 186180-25-6P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(identification of novel **mdm2** binding peptides by phage display)

ATTN: Barb O'Bryen

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

# SEARCH REQUEST FORM

10/14583
CRF

Requestor's Name: (STIC) JANE ZARA

Serial Number: 09/214,371

Date: 2-18-04

Phone: 2-0765

Art Unit: 1635

**Search Topic:**

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search

seq 10 - 8
11 - 9
35 - 10
36 - 10

10 & 11 AAs Seq ID Nos.

as described in claims

35 + 36

- No size limit
- size limit to 20 AA

Thanks.

No interference please.

**STAFF USE ONLY**

Date completed: 2-20-04
Searcher: BOB
Terminal time: 40
Elapsed time: prep 90
CPU time:
Total time:
Number of Searches:
Number of Databases: 7

**Search Site**

- STIC
- CM-1
- Pre-S

**Type of Search**

- N.A. Sequence
- 4 A.A. Sequence
- Structure
- Bibliographic

**Vendors**

- IG Suite
- 275 STN
- Dialog
- APS
- Geninfo
- SDC
- DARC/Questel
- Other